

09/06/627

=> d his

(FILE 'HOME' ENTERED AT 11:59:47 ON 12 NOV 2004)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 12:00:12 ON 12 NOV 2004

L1 1253188 S KINASE?  
L2 182160 S HISTIDINE  
L3 4732 S L1(A) L2  
L4 6785689 S CLON? OR EXPRESS? OR RECOMBINANT  
L5 249014 S STAPHYLOCOCCUS (A) AUREUS  
L6 163 S L3 AND L5  
L7 102 S L4 AND L6  
L8 58 DUP REM L7 (44 DUPLICATES REMOVED)  
E WALLIS N G/AU  
L9 119 S E3  
E SHILLING L K/AU  
L10 93 S E3-E9  
E MOONEY J L/AU  
L11 63 S E3  
E DEBOUCK C/AU  
L12 416 S E3  
L13 612 S E3-E8  
E ZHONG Y Y/AU  
L14 40 S E3  
E JAWORSKI D D/AU  
L15 276 S E3-E10  
E WANG M/AU  
L16 6684 S E3  
E THROUP J P/AU  
L17 115 S E3-E7  
L18 7894 S L8 OR L9 OR L10 OR L11 OR L13 OR L14 OR L15 OR L16 OR L  
L19 72 S L6 AND L18  
L20 59 DUP REM L19 (13 DUPLICATES REMOVED)

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FILE 'MEDLINE' ENTERED AT 12:00:12 ON 12 NOV 2004

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=> s kinase?

L1 1253188 KINASE?

=> s histidine

L2 182160 HISTIDINE

=> s l1(a)l2

L3 4732 L1(A) L2

=> s clon? or express? or recombinant

4 FILES SEARCHED...

L4 6785689 CLON? OR EXPRESS? OR RECOMBINANT

=> s staphylococcus (a)aureus

L5 249014 STAPHYLOCOCCUS (A) AUREUS

=> s l3 and l5

L6 163 L3 AND L5

=> s l4 and l6

L7 102 L4 AND L6

=> dup rem 17

PROCESSING COMPLETED FOR L7

L8 58 DUP REM L7 (44 DUPLICATES REMOVED)

=> d 1-58 ibib ab

L8 ANSWER 1 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on  
STN

ACCESSION NUMBER: 2004:517041 SCISEARCH

THE GENUINE ARTICLE: 824CT

TITLE: Identification of a novel two-component system in  
Streptococcus gordonii V288 involved in biofilm formation

AUTHOR: Zhang Y S; Lei Y; Khammanivong A; Herzberg M C (Reprint)

CORPORATE SOURCE: Univ Minnesota, Dept Oral Sci, 17-164 Moos Tower, 515

Delaware St SE, Minneapolis, MN 55455 USA (Reprint); Univ Minnesota, Dept Oral Sci, Minneapolis, MN 55455 USA; Univ Minnesota, Mucosal & Vaccine Res Ctr, Minneapolis, MN 55455 USA; Univ Minnesota, Sch Dent, Dept Oral Sci, Minneapolis, MN 55455 USA

COUNTRY OF AUTHOR:

USA

SOURCE:

INFECTION AND IMMUNITY, (JUN 2004) Vol. 72, No. 6, pp. 3489-3494.

Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.

ISSN: 0019-9567.

DOCUMENT TYPE:

Article; Journal

LANGUAGE:

English

REFERENCE COUNT:

40

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB *Streptococcus gordonii* is a pioneer colonizer of the teeth, contributing to the initiation of the oral biofilm called dental plaque. To identify genes that may be important in biofilm formation, a plasmid integration library of *S. gordonii* V288 was used. After screening for *in vitro* biofilm formation on polystyrene, a putative biofilm-defective mutant was isolated. In this mutant, pAK36 was inserted into a locus encoding a novel two-component system (bfr [biofilm formation related]) with two cotranscribed genes that form an operon. bfrA encodes a putative response regulator, while bfrB encodes a receptor histidine kinase. The bfr mutant and wild-type strain V288 showed similar growth rates in Todd-Hewitt broth (THB). A bfr-cat fusion strain was constructed. During growth in THB, the reporter activity (chloramphenicol acetyltransferase) was first detected in mid-log phase and reached a maximum in stationary phase, suggesting that transcription of bfr was growth stage dependent. After being harvested from THB, the bfr mutant adhered less effectively than did wild-type strain V288 to saliva-coated hydroxyapatite (sHA). To simulate pioneer colonization of teeth, *S. gordonii* V288 was incubated with sHA for 4 h in THB with 10% saliva to develop biofilms. RNA was isolated, and expression of bfrAB was estimated. In comparison to that of cells grown in suspension (free-growing cells), bfr mRNA expression by sessile cells on sHA was 1.8-fold greater and that by surrounding planktonic cells was 3.5-fold greater. Therefore, bfrAB is a novel two-component system regulated in association with *S. gordonii* biofilm formation *in vitro*.

L8 ANSWER 2 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2004:498290 SCISEARCH

THE GENUINE ARTICLE: 822TE

TITLE: Differential gene expression in response to hydrogen peroxide and the putative PerR regulon of *Synechocystis* sp strain PCC 6803

AUTHOR: Li H; Singh A K; McIntyre L M; Sherman L A (Reprint)

CORPORATE SOURCE: Purdue Univ, Dept Biol Sci, W Lafayette, IN 47907 USA (Reprint); Purdue Univ, Dept Agron, W Lafayette, IN 47907 USA

COUNTRY OF AUTHOR:

USA

SOURCE: JOURNAL OF BACTERIOLOGY, (JUN 2004) Vol. 186, No. 11, pp. 3331-3345.

Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.

ISSN: 0021-9193.

DOCUMENT TYPE:

Article; Journal

LANGUAGE:

English

REFERENCE COUNT:

75

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB We utilized a full genome cDNA microarray to identify the genes that comprise the peroxide stimulon in the cyanobacterium *Synechocystis* sp. strain PCC 6803. We determined that a gene (slr1738) encoding a protein

similar to PerR in *Bacillus subtilis* was induced by peroxide. We constructed a PerR knockout strain and used it to help identify components of the PerR regulon, and we found that the regulatory properties were consistent with the hypothesis that PerR functions as a repressor. This effort was guided by finding putative PerR boxes in positions upstream of specific genes and by careful statistical analysis. PerR and sll1621 (ahpC), which codes for a peroxiredoxin, share a divergent promoter that is regulated by PerR. We found that isiA, encoding a Chl protein that is induced under low-iron conditions, was strongly induced by a short-term peroxide stress. Other genes that were strongly induced by peroxide included sigD, sigB, and genes encoding peroxiredoxins and Dsb-like proteins that have not been studied yet in this strain. A gene (slr1894) that encoded a protein similar to MrgA in *B. subtilis* was upregulated by peroxide, and a strain containing an mrgA knockout mutation was highly sensitive to peroxide. A number of genes were downregulated, including key genes in the chlorophyll biosynthesis pathway and numerous regulatory genes, including those encoding **histidine kinases**. We used PerR mutants and a thioredoxin mutant (TrxA1) to study differential expression in response to peroxide and determined that neither PerR nor TrxA1 is essential for the peroxide protective response.

L8 ANSWER 3 OF 58 MEDLINE on STN DUPLICATE 1  
ACCESSION NUMBER: 2004166238 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 15060046  
TITLE: Characterization of virulence factor regulation by SrrAB, a two-component system in *Staphylococcus aureus*.  
AUTHOR: Pragman Alexa A; Yarwood Jeremy M; Tripp Timothy J; Schlievert Patrick M  
CORPORATE SOURCE: Department of Microbiology, University of Minnesota Medical School, Minneapolis, Minnesota 55455, USA.  
CONTRACT NUMBER: T32 AI 07421 (NIAID)  
SOURCE: Journal of bacteriology, (2004 Apr) 186 (8) 2430-8.  
Journal code: 2985120R. ISSN: 0021-9193.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-AF260326  
ENTRY MONTH: 200405  
ENTRY DATE: Entered STN: 20040403  
Last Updated on STN: 20040525  
Entered Medline: 20040524  
AB Workers in our laboratory have previously identified the staphylococcal respiratory response AB (SrrAB), a *Staphylococcus aureus* two-component system that acts in the global regulation of virulence factors. This system down-regulates production of agr RNAIII, protein A, and toxic shock syndrome toxin 1 (TSST-1), particularly under low-oxygen conditions. In this study we investigated the localization and membrane orientation of SrrA and SrrB, transcription of the srrAB operon, the DNA-binding properties of SrrA, and the effect of SrrAB expression on *S. aureus* virulence. We found that SrrA is localized to the *S. aureus* cytoplasm, while SrrB is localized to the membrane and is properly oriented to function as a **histidine kinase**. srrAB has one transcriptional start site which results in either an srrA transcript or a full-length srrAB transcript; srrB must be cotranscribed with srrA. Gel shift assays of the agr P2, agr P3, protein A (spa), TSST-1 (tst), and srr promoters revealed SrrA binding at each of these promoters. Analysis of SrrAB-overexpressing strains by using the rabbit model of bacterial endocarditis demonstrated that overexpression of SrrAB decreased the virulence of the organisms compared to the virulence of isogenic strains that do not overexpress SrrAB. We concluded that SrrAB is properly localized and oriented to function as a two-component system. Overexpression of SrrAB, which represses agr RNAIII, TSST-1, and protein A

in vitro, decreases virulence in the rabbit endocarditis model. Repression of these virulence factors is likely due to a direct interaction between SrrA and the agr, tst, and spa promoters.

L8 ANSWER 4 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2004:271816 SCISEARCH

THE GENUINE ARTICLE: 802HO

TITLE: pbp2229-mediated nisin resistance mechanism in *Listeria monocytogenes* confers cross-protection to class IIa bacteriocins and affects virulence gene **expression**

AUTHOR: Gravesen A (Reprint); Kallipolitis B; Holmstrom K; Hoiby P E; Ramnath M; Knochel S

CORPORATE SOURCE: Royal Vet & Agr Univ, LMC, Ctr Adv Food Studies, Dept Dairy & Food Sci, Rolighedsvej 30, DK-1958 Frederiksberg C, Denmark (Reprint); Royal Vet & Agr Univ, LMC, Ctr Adv Food Studies, Dept Dairy & Food Sci, DK-1958 Frederiksberg C, Denmark; Univ So Denmark, Dept Biochem & Mol Biol, DK-5230 Odense, Denmark; Bioneer A S, Dept Mol Characterizat, DK-2970 Horsholm, Denmark; Univ Stellenbosch, Dept Biochem, ZA-7602 Matieland, South Africa

COUNTRY OF AUTHOR: Denmark; South Africa

SOURCE: APPLIED AND ENVIRONMENTAL MICROBIOLOGY, (MAR 2004) Vol. 70, No. 3, pp. 1669-1679.

Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.

ISSN: 0099-2240.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 50

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB It was previously shown that enhanced nisin resistance in some mutants was associated with increased **expression** of three genes, pbp2229, hpk1021, and Imo2487, encoding a penicillin-binding protein, a **histidine kinase** and a protein of unknown function, respectively. In the present work, we determined the direct role of the three genes in nisin resistance. Interruption of pbp2229 and hpk1021 eliminated the nisin resistance phenotype. Interruption of hpk1021 additionally abolished the increase in pbp2229 **expression**. The results indicate that this nisin resistance mechanism is caused directly by the increase in pbp2229 **expression**, which in turn is brought about by the increase in hpk1021 **expression**. We also found a degree of cross-protection between nisin and class IIa bacteriocins and investigated possible mechanisms. The **expression** of virulence genes in one nisin-resistant mutant and two class IIa bacteriocin-resistant mutants of the same wild-type strain was analyzed, and each mutant consistently showed either an increase or a decrease in the **expression** of virulence genes (prfA-regulated as well as prfA-independent genes). Although the changes mostly were moderate, the consistency indicates that a mutant-specific change in virulence may occur concomitantly with bacteriocin resistance development.

L8 ANSWER 5 OF 58 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2004212976 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15109784

TITLE: Regulation of virulence determinants in *Staphylococcus aureus*: complexity and applications.

AUTHOR: Bronner Stephane; Monteil Henri; Prevost Gilles

CORPORATE SOURCE: Institut de Bacteriologie, Faculte de Medecine, Universite Louis Pasteur - Hopitaux, Universitaires de Strasbourg, 3, rue Koeberle, F-67000 Strasbourg, France.

SOURCE: FEMS microbiology reviews, (2004 May) 28 (2) 183-200. Ref:

JOURNAL CODE: 8902526. ISSN: 0168-6445.

PUB. COUNTRY:

Netherlands

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, ACADEMIC)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

200407

ENTRY DATE:

Entered STN: 20040428

Last Updated on STN: 20040703

Entered Medline: 20040702

AB The virulence of *Staphylococcus aureus* is essentially determined by cell wall associated proteins and secreted toxins that are regulated and expressed according to growth phases and/or growth conditions. Gene expression is regulated by specific and sensitive mechanisms, most of which act at the transcriptional level. Regulatory factors constitute numerous complex networks, driving specific interactions with target gene promoters. These factors are largely regulated by two-component regulatory systems, such as the agr, saeRS, srrAB, arlSR and lytRS systems. These systems are sensitive to environmental signals and consist of a sensor histidine kinase and a response regulator protein. DNA-binding proteins, such as SarA and the recently identified SarA homologues (SarR, Rot, Sars, SarT, SarU), also regulate virulence factor expression. These homologues might be intermediates in the regulatory networks. The multiple pathways generated by these factors allow the bacterium to adapt to environmental conditions rapidly and specifically, and to develop infection. Precise knowledge of these regulatory mechanisms and how they control virulence factor expression would open up new perspectives for antimicrobial chemotherapy using key inhibitors of these systems.

L8 ANSWER 6 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2004:139965 SCISEARCH

THE GENUINE ARTICLE: 769FL

TITLE: Regulation of virulence determinants in vitro and in vivo in *Staphylococcus aureus*

AUTHOR: Cheung A L (Reprint); Bayer A S; Zhang G Y; Gresham H; Xiong Y Q

CORPORATE SOURCE: Dartmouth Coll Sch Med, Dept Microbiol, Hanover, NH 03755 USA (Reprint); Univ Calif Los Angeles, Harbor Med Ctr, Res & Educ Inst, Torrance, CA 90502 USA; Univ Calif Los Angeles, Sch Med, Los Angeles, CA 90024 USA; Natl Jewish Med & Res Ctr, Integrated Dept Immunol, Denver, CO 80206 USA; Univ New Mexico, Sch Med, Dept Microbiol & Mol Genet, Albuquerque, NM 87131 USA

COUNTRY OF AUTHOR: USA

SOURCE: FEMS IMMUNOLOGY AND MEDICAL MICROBIOLOGY, (15 JAN 2004)

Vol. 40, No. 1, pp. 1-9.

Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.

ISSN: 0928-8244.

DOCUMENT TYPE: General Review; Journal

LANGUAGE: English

REFERENCE COUNT: 53

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB *Staphylococcus aureus* is an opportunistic pathogen.

In response to changing host environments, this bacterium has the capability to switch on selective sets of genes to enhance its chances for survival. This switching process is precisely controlled by global regulatory elements. There are two major groups of global regulatory elements in *S. aureus*, including two-component regulatory systems (TCRSSs)

and the SarA protein family. Presumably, the sensor proteins of the 16 TCRSSs in *S. aureus* provide external sensing, while the response regulators, in conjunction with alternative transcription factors and the SarA protein family, function as effectors within the intricate regulatory network to respond to environmental stimuli. Sequence alignment and structural data indicate that the SarA protein family could be subdivided into three subfamilies: (1) single-domain proteins; (2) double-domain proteins; and (3) proteins homologous to the MarR protein family. Recent data using reporter gene fusions in animal models, have confirmed distinct expression profiles of selected regulatory and target genes in vitro vs. in vivo. (C) 2003 Federation of European Microbiological Societies. Published by Elsevier B.V. All rights reserved.

L8 ANSWER 7 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2004-00275 BIOTECHDS

TITLE: New isolated nucleic acid encoding a peptide that kills both wild type pneumococci and a strain of *Pneumococcus* that is autolysin deficient, useful for treating or preventing bacterial infections or inflammations;  
recombinant protein production for use in disease therapy and drug screening

AUTHOR: NOVAK R; TUOMANEN E I

PATENT ASSIGNEE: ST JUDE CHILDREN'S RES HOSPITAL

PATENT INFO: US 6630583 7 Oct 2003

APPLICATION INFO: US 2000-493940 28 Jan 2000

PRIORITY INFO: US 2000-493940 28 Jan 2000; US 1998-84399 6 May 1998

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2003-810553 [76]

AB DERWENT ABSTRACT:

NOVELTY - A new isolated nucleic acid (I) encoding a peptide comprises: the amino acid sequence selected from an amino acid sequence having 25 amino acids (P1) or (P1) with a conservative amino acid substitution; or 7-100 amino acids comprising three contiguous amino acids from (P1), where the peptide kills both wild type pneumococci, and a strain of *Pneumococcus* that is autolysin deficient.

WIDER DISCLOSURE - Also disclosed are: (1) an antibody against any of the proteins or peptides of the invention; (2) a pharmaceutical composition comprising one or more of the peptides and a pharmaceutical carrier; (3) a method of treating or preventing bacterial infections or inflammations; (4) a method for identifying peptides or agents capable of killing and/or inhibiting the growth of a strain of bacteria; (5) a method of identifying a cell that contains a mutation in a histidine kinase gene, in a response regulator gene or in a component of a gene for the ABC transporter system; (6) a peptide that acts synergistically with antibiotics that are active against bacterial cell walls; (7) a method of producing a peptide by chemical synthesis or recombinant technology; (8) a method of testing putative peptide antibiotics to identify new agents useful in preventing bacterial proliferation and/or causing cell death or lysis; (9) a method of designing putative peptide antibiotics through altering the amino acid and/or nucleic acid sequences of a peptide encoded by an open reading frame; and (10) a method of detecting and/or identifying penicillin or vancomycin tolerant bacterial strains.

BIOTECHNOLOGY - Preferred Peptide: The peptide encoded by the nucleic acid consist of 12-50 amino acids, preferably 25-35 amino acids or 17-35 amino acids.

ACTIVITY - Antibacterial; Antiinflammatory; Gynecological; Antitubercular; Tuberculostatic. No biological data given.

MECHANISM OF ACTION - None given.

USE - (I) is useful in preventing or treating disease caused by a bacterium, e.g. *Staphylococcus aureus*, *Acinetobacter*, *Enterococcus faecalis*, *Escherichia coli*, *Pseudomonas aeruginosa*, which all causes blood poisoning, *Mycobacterium tuberculosis* which causes

tuberculosis, *Shigella dysenteriae* which causes dysentery, *Neisseria gonorrhoeae* which causes gonorrhoea and *Streptococcus pneumoniae* which causes blood poisoning, middle ear infections, pneumonia or meningitis in humans. The peptides can be employed as a preservative or as part of a composition used as a preservative. It can also be used as a laboratory tool, e.g. in conjunction with one or more bacteria; drug selection markers.

**ADMINISTRATION** - The composition comprising the peptides can be administered topically, parenterally (intravenous injection, intra-arteriole, intramuscular, intradermal, subcutaneous, intraperitoneal, intraventricular or intracranial), transmucosally (orally, nasally or rectally) or transdermally. No dosage given.

**EXAMPLE** - Genome analysis was performed using FASTA, TFASTA, BLAST and BLASTN programs. A nucleotide sequence having 75 bp or amino acid sequence having 25 amino acids were used to search existing public databases containing the multiple bacterial genomes. Homologues were found in *Methanococcus*, *Haemophilus*, *Archlaeoglobus*, *Borrelia* and *Synechocystis*. Cell growth curves were performed in the presence or absence of the test reagents. Samples were prepared as follows: 1 ml of *Pneumococcus* culture was placed into 10 ml of prewarmed Semisynthetic (C+Y) medium. The optical density (OD) of the bacteria was monitored at 620 nm until an OD of approximately 0.1 was reached. At this point the test reagents were administered to the samples. The cells were cultured for up to 11 hours at 37 degrees Centigrade and the OD at 620 nm was monitored every hour. A decrease in OD<sub>620</sub> is indicative of cell lysis, an increase is indicative of bacterial growth. No change in optical density indicates bacterial growth. The open reading frames in a gene cluster encoding an ABC transporter and a two component His-Asp phosphorelay pathway of *Streptococcus pneumoniae* were examined in pursuit of a putative peptide that might be involved in autolysis. A short open reading frame was located between ORFW1-W3 and RR/HK at approximately position 6500. This short open reading frame (P) has a nucleotide sequence having 75 bp and encodes a peptide having an amino acid sequence with 25 amino acids. The peptide having 25 amino acids was chemically synthesized and tested for growth inhibiting, killing and lytic activity in *Streptococcus pneumoniae* cultures. (152 pages)

L8 ANSWER 8 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2003-18374 BIOTECHDS

**TITLE:** New oligonucleotide probes which specifically hybridize to *Staphylococcus aureus histidine kinase* essential genes, useful for developing antibacterial agents, or as probes for detecting the presence a particular gene; drug screening for use in bacterium infection diagnosis and gene therapy

**AUTHOR:** BENTON B; MALOUIN F; MARTIN P K; SCHMID M B; SUN D

**PATENT ASSIGNEE:** ESSENTIAL THERAPEUTICS INC

**PATENT INFO:** US 6514746 4 Feb 2003

**APPLICATION INFO:** US 1998-82077 20 May 1998

**PRIORITY INFO:** US 1998-82077 20 May 1998; US 1995-3798 15 Sep 1995

**DOCUMENT TYPE:** Patent

**LANGUAGE:** English

**OTHER SOURCE:** WPI: 2003-478763 [45]

**AB** DERWENT ABSTRACT:

**NOVELTY** - An oligonucleotide probe at least 15 nucleotides in length which specifically hybridizes to a nucleotide which is the same as or complementary to a DNA comprising a sequence of 3731 (I), 702 (II) or 1827 (III) bp given in the specification, especially to (II) and (III).

**DETAILED DESCRIPTION** - An INDEPENDENT CLAIM is also included for a recombinant bacterial cell containing an artificially inserted DNA construct comprising a nucleotide base sequence which is the same as or complementary to a nucleotide base sequence of the coding region of (I), (II) or (III).

WIDER DISCLOSURE - Also disclosed are the following: (1) screening for an antibacterial agent by determining whether a test compound is active against (I), (II) or (III); (2) diagnosing the presence of a bacterial strain having (I), (II) or (III); (3) treating a bacterial infection in a mammal by administering a compound active against a bacterial gene selected from (I), (II) and (III); and (4) *Staphylococcus aureus* genes termed aspA and espB comprising sequences of 702 and 1827 base pairs respectively.

BIOTECHNOLOGY - Preferred Probe: The coding region comprises (II) or (III).

ACTIVITY - Antibacterial. No supporting data provided.

MECHANISM OF ACTION - Gene therapy.

USE - The probes are useful for the development of antibacterial agents, as probes for identifying the presence of a gene or a bacterium having the particular gene, as reagents to identify DNA chains which contain a sequence corresponding to the probe (e.g. for identifying clones having a recombinant DNA insert), and as PCR primers.

ADMINISTRATION - Dosage is 0.1-100 mug/ml. Administration can be through oral, rectal, transdermal, vaginal, transmucosal, intestinal, or parenteral (e.g. intramuscular, subcutaneous, intramedullary, intrathecal, intraventricular, intravenous, intraperitoneal, intranasal or intraocular) routes.

EXAMPLE - No relevant example given. (35 pages)

L8 ANSWER 9 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2003:1087573 SCISEARCH

THE GENUINE ARTICLE: 751GL

TITLE: Chemical communication among bacteria

AUTHOR: Taga M E; Bassler B L (Reprint)

CORPORATE SOURCE: Princeton Univ, Dept Mol Biol, Princeton, NJ 08544 USA (Reprint)

COUNTRY OF AUTHOR: USA

SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (25 NOV 2003) Vol. 100, Supp. [2], pp. 14549-14554.

Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418 USA.

ISSN: 0027-8424.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 65

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Cell-cell communication in bacteria is accomplished through the exchange of chemical signal molecules called autoinducers. This process, called quorum sensing, allows bacteria to monitor their environment for the presence of other bacteria and to respond to fluctuations in the number and/or species present by altering particular behaviors. Most quorum-sensing systems are species- or group-specific, which presumably prevents confusion in mixed-species environments. However, some quorum-sensing circuits control behaviors that involve interactions among bacterial species. These quorum-sensing circuits can involve both intra- and interspecies communication mechanisms. Finally, anti-quorum-sensing strategies are present in both bacteria and eukaryotes, and these are apparently designed to combat bacteria that rely on cell-cell communication for the successful adaptation to particular niches.

L8 ANSWER 10 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2003:224073 SCISEARCH

THE GENUINE ARTICLE: 652DR

TITLE: Detection of secreted peptides by using hypothesis-driven multistage mass spectrometry

AUTHOR: Kalkum M; Lyon G J; Chait B T (Reprint)  
CORPORATE SOURCE: Rockefeller Univ, Lab Mass Spectrometry & Gaseous Chem,  
1230 York Ave, New York, NY 10021 USA (Reprint);  
Rockefeller Univ, Lab Mass Spectrometry & Gaseous Chem,  
New York, NY 10021 USA; Rockefeller Univ, Selma & Lawrence  
Ruben Lab Synthet Prot Chem, New York, NY 10021 USA  
COUNTRY OF AUTHOR: USA  
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE  
UNITED STATES OF AMERICA, (4 MAR 2003) Vol. 100, No. 5,  
pp. 2795-2800.  
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW,  
WASHINGTON, DC 20418 USA.  
ISSN: 0027-8424.

DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 53

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB A method is presented for the rapid detection and characterization of trace amounts of peptides secreted from microorganisms, including pheromones, virulence factors, and quorum-sensing peptides. The procedure, based on targeted multistage MS, uses a novel matrix-assisted laser desorption/ionization-ion trap mass spectrometer to overcome limitations of current MS methods (limited dynamic range, signal suppression effects, and chemical noise) that impair observation of low abundance peptides from complex biological matrixes. Here, secreted peptides that are hypothesized to be present in the supernatant, but that may not be sufficiently abundant to be observed in single-stage mass spectra, are subjected to multistage MS. Highly specific fragmentation signatures enable unambiguous identification of the peptides of interest and differentiation of the signals from the background. As examples, we demonstrate the rapid (<1 min) determination of the mating type of cells in colonies of *Saccharomyces cerevisiae* and the elucidation of autoinducing peptides (AIPs) from supernatants of pathogenic *Staphylococci*. We confirm the primary structures of the agrD encoded cyclic AIPs of *Staphylococcus aureus* for groups I, II, and IV and provide direct evidence that the native group-III AIP is a heptapeptide (INCDFL). We also show that the homologous peptide from *Staphylococcus intermedius* is a nonapeptide (RIPTSTGFF) with a lactone ring formed through condensation of the serine side chain with the C terminus of the peptide. This is the first demonstration of cyclization in a staphylococcal AIP that occurs via lactone formation. These examples demonstrate the analytical power of the present procedure for characterizing secreted peptides and its potential utility for identifying microorganisms.

L8 ANSWER 11 OF 58 MEDLINE on STN DUPLICATE 3  
ACCESSION NUMBER: 2003570426 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 14651645  
TITLE: Constitutive expression of PcsB suppresses the requirement for the essential VicR (YycF) response regulator in *Streptococcus pneumoniae* R6.  
AUTHOR: Ng Wai-Leung; Robertson Gregory T; Kazmierczak Krystyna M; Zhao Jingyong; Gilmour Raymond; Winkler Malcolm E  
CORPORATE SOURCE: Department of Biology, Indiana University, Jordan Hall 142, Bloomington, IN 47405, USA.  
SOURCE: Molecular microbiology, (2003 Dec) 50 (5) 1647-63.  
Journal code: 8712028. ISSN: 0950-382X.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200403  
ENTRY DATE: Entered STN: 20031216  
Last Updated on STN: 20040302

Entered Medline: 20040301

AB We report several new findings about the function of the essential VicRK two-component regulatory system (TCS) in the human pathogen *Streptococcus pneumoniae*. The *vicR*-encoded response regulator, *vicK*-encoded histidine kinase and the protein encoded by the downstream *vicX* gene are the homologues of the *YycF*, *YycG* and *YycJ* proteins, respectively, studied previously in *Bacillus subtilis* and *Staphylococcus aureus*. Using a regulatable promoter, we demonstrated that the *VicK histidine kinase* is conditionally required for growth of *S. pneumoniae*. Likewise, we found that the *VicX* protein is also conditionally required for growth and probably plays a role in the essential signal transduction pathway mediated by *VicR* and *VicK*. Recovery of limited substitutions in the conserved aspartate 52 residue (D52) of *VicR* was consistent with a requirement for phosphorylation of *VicR* for growth under some conditions. We applied microarrays to characterize the changes in transcription patterns in bacteria depleted for *vicRKX* operon expression. Our results suggest that the *pcrB* gene is a target of the *VicRK* TCS. We present evidence that downregulation of *pcrB* could account for many of the defects in cell growth, shape, size and morphology observed in bacteria depleted for *vicRKX* expression. Furthermore, constitutive expression of *pcrB* suppressed the essential requirement for the *VicRK* TCS and allowed the isolation of *vicR* null mutants.

L8 ANSWER 12 OF 58 HCPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:776164 HCPLUS

DOCUMENT NUMBER: 139:359758

TITLE: Genes controlled by the essential *YycG/YycF* two-component system of *Bacillus subtilis* revealed through a novel hybrid regulator approach

AUTHOR(S): Howell, Alistair; Dubrac, Sarah; Andersen, Kasper Krogh; Noone, David; Fert, Juliette; Msadek, Tarek; Devine, Kevin

CORPORATE SOURCE: Department of Genetics, Smurfit Institute, Trinity College Dublin, Dublin, 2, Ire.

SOURCE: Molecular Microbiology (2003), 49(6), 1639-1655  
CODEN: MOMIEE; ISSN: 0950-382X

PUBLISHER: Blackwell Publishing Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The *YycG/YycF* two-component system, originally identified in *Bacillus subtilis*, is very highly conserved and appears to be specific to low G + C Gram-pos. bacteria. This system is required for cell viability, although the basis for this and the nature of the *YycF* regulon remained elusive. Using a combined hybrid regulator/transcriptome approach involving the inducible expression of a *PhoP*'-'*YycF* chimerical protein in *B. subtilis*, the authors have shown that expression of *yocH*, which encodes a potential autolysin, is specifically activated by *YycF*. Gel mobility shift and DNase I footprinting assays were used to show direct binding in vitro of purified *YycF* to the regulatory regions of *yocH* as well as *ftsAZ*, previously reported to be controlled by *YycF*. Nucleotide sequence anal. and site-directed mutagenesis allowed the authors' to define a potential consensus recognition sequence for the *YycF* response regulator, composed of two direct repeats: 5'-TGT A/T A A/T/C-N5-TGT A/T A A/T/C-3'. A DNA-motif anal. indicates that there are potentially up to 10 genes within the *B. subtilis* *YycG/YycF* regulon, mainly involved in cell wall metabolism and membrane protein synthesis. Among these, *YycF* was shown to bind directly to the region upstream from the *ykvt* gene, encoding a potential cell wall hydrolase, and the intergenic region of the *tagAB/tagDEF* divergon, encoding essential components of teichoic acid biosynthesis. Definition of a potential *YycF* recognition sequence allowed the authors' to identify likely members of the *YycF* regulon in other low G + C Gram-pos. bacteria, including several pathogens such as *Listeria monocytogenes*, *Staphylococcus aureus* and *Streptococcus*

pneumoniae.  
REFERENCE COUNT: 63

THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN  
ACCESSION NUMBER: 2003:513309 SCISEARCH  
THE GENUINE ARTICLE: 687GZ  
TITLE: Autoinduction and signal transduction in the regulation of staphylococcal virulence  
AUTHOR: Novick R P (Reprint)  
CORPORATE SOURCE: NYU, Sch Med, Dept Microbiol, Skirball Inst, Program Mol Pathogenesis, New York, NY 10016 USA (Reprint); NYU, Sch Med, Dept Med, Skirball Inst, Program Mol Pathogenesis, New York, NY 10016 USA  
COUNTRY OF AUTHOR: USA  
SOURCE: MOLECULAR MICROBIOLOGY, (JUN 2003) Vol. 48, No. 6, pp. 1429-1449.  
Publisher: BLACKWELL PUBLISHING LTD, 9600 GARSINGTON RD, OXFORD OX4 2DG, OXON, ENGLAND.  
ISSN: 0950-382X.  
DOCUMENT TYPE: General Review; Journal  
LANGUAGE: English  
REFERENCE COUNT: 126

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB The accessory genes of *Staphylococcus aureus*, including those involved in pathogenesis, are controlled by a complex regulatory network that includes at least four two-component systems, one of which, agr, is a quorum sensor, an alternative sigma factor and a large set of transcription factors, including at least two of the superantigen genes, tst and seb. These regulatory genes are hypothesized to act in a time- and population density-dependent manner to integrate signals received from the external environment with the internal metabolic machinery of the cell, in order to achieve the production of particular subsets of accessory/virulence factors at the time and in quantities that are appropriate to the needs of the organism at any given location. From the standpoint of pathogenesis, the regulatory agenda is presumably tuned to particular sites in the host organism. To address this hypothesis, it will be necessary to understand in considerable detail the regulatory interactions among the organism's numerous controlling systems. This review is an attempt to integrate a large body of data into the beginnings of a model that will hopefully help to guide research towards a full-scale test.

L8 ANSWER 14 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2004-03939 BIOTECHDS  
TITLE: Isolation and characterization of inhibitors of the essential histidine kinase, YycG in *Bacillus subtilis* and *Staphylococcus aureus*; vector-mediated gene transfer and expression in host cell for antibiotic screening and antibiotic-resistant bacterium infection therapy  
AUTHOR: WATANABE T; HASHIMOTO Y; YAMAMOTO K; HIRAO K; ISHIHAMA A; HINO M; UTSUMI R  
CORPORATE SOURCE: Kinki Univ; Nippon Inst Biol Sci; Fujisawa Pharmaceut Co Ltd  
LOCATION: Utsumi R, Kinki Univ, Grad Sch Agr, Dept Biosci and Biotechnol, 3327-204 Nakamachi, Nara 6318505, Japan  
SOURCE: JOURNAL OF ANTIBIOTICS; (2003) 56, 12, 1045-1052  
ISSN: 0021-8820  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB AUTHOR ABSTRACT - The set of sensor kinase YycG and response regulator YycF is the only essential two-component system (TCS) in *Bacillus subtilis* and *Staphylococcus aureus*. We have developed

a screening method for antibacterial agents that inhibit YycG, the essential histidine kinase (HK). To increase screening sensitivity, a temperature-sensitive yycF mutant (CNM2000) of *B. subtilis* with super-sensitivity to HK inhibitors was constructed, which was used for the screening of acetone extracts from 4000 microbes. A total of 11 samples showed higher sensitivity to CNM2000 than to wild-type parent 168, and seven of those were characterized to be potent inhibitors against autophosphorylation of YycG. One sample compound was purified and identified as aranorosinol B, a known antibacterial agent against Gram-positive bacteria including *B. subtilis* and *S. aureus*. Aranorosinol B inhibited YycG from both *B. subtilis* and *S. aureus* with a half-maximum inhibitory concentration (IC50) of 223 and 211 μm, respectively. (8 pages)

L8 ANSWER 15 OF 58 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2003448363 EMBASE  
TITLE: Turning virulence on and off in *Staphylococci*.  
AUTHOR: Muir T.W.  
CORPORATE SOURCE: Dr. T.W. Muir, Lab. of Synthetic Protein Chemistry, The Rockefeller University, 1230 York Avenue, New York, NY 10021, United States. muirt@rockefeller.edu  
SOURCE: Journal of Peptide Science, (2003) 9/10 (612-619).  
Refs: 21  
ISSN: 1075-2617 CODEN: JPSIEI  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 004 Microbiology  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB The progress made in a multidisciplinary research programme designed to elucidate the molecular basis of the interaction of *Staphylococcus aureus* secreted autoinducing peptides (AIPs) with their respective cell surface receptors is reviewed. Copyright .COPYRGT. 2003 European Peptide Society and John Wiley & Sons, Ltd.

L8 ANSWER 16 OF 58 MEDLINE on STN DUPLICATE 4  
ACCESSION NUMBER: 2003373501 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12867749  
TITLE: Biochemical characterization of the first essential two-component signal transduction system from *Staphylococcus aureus* and *Streptococcus pneumoniae*.  
AUTHOR: Clausen Valerie A; Bae Weonhye; Throup John; Burnham Martin K R; Rosenberg Martin; Wallis Nicola G  
CORPORATE SOURCE: Antimicrobials and Host Defense, GlaxoSmithKline Pharmaceuticals, Collegeville, PA, USA.  
SOURCE: Journal of molecular microbiology and biotechnology, (2003) 5 (4) 252-60.  
Journal code: 100892561. ISSN: 1464-1801.  
PUB. COUNTRY: Switzerland  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200309  
ENTRY DATE: Entered STN: 20030812  
Last Updated on STN: 20030905  
Entered Medline: 20030904

AB The YYCFG two-component signal transduction system (TCSTS) has been shown to be essential to the viability of several gram-positive bacteria. However, the function of the gene pair remains unknown. Interestingly, while both components are essential to *Staphylococcus aureus* and *Bacillus subtilis*, only the response regulator (YYCF)

is essential to *Streptococcus pneumoniae*. To study this essential TCSTS further, the *S. pneumoniae* and *S. aureus* truncated YycG histidine kinase and full-length YycF response regulator proteins were characterized at a biochemical level. The recombinant proteins from both organisms were expressed in *Escherichia coli* and purified. The YycG autophosphorylation activities were activated by ammonium. The apparent  $K(m)$  (ATP) of *S. aureus* YycG autophosphorylation was 130 microM and *S. pneumoniae* was 3.0 microM. Each had similar  $K(cat)$  values of 0.036 and 0.024 min<sup>-1</sup>, respectively. Cognate phosphotransfer was also investigated indicating different levels of the phosphorylated YycG intermediates during the reaction. The *S. pneumoniae* YycG phosphorylated intermediate was not detectable in the presence of its cognate YycF, while phosphorylated *S. aureus* YycG and YycF were detected concurrently. In addition, noncognate phosphotransfer was demonstrated between the two species. These studies thoroughly compare the essential YycFG TCSTS from the two species at the biochemical level and also establish methods for assaying the activities of these antibacterial targets.

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L8 ANSWER 17 OF 58 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2003:517200 BIOSIS

DOCUMENT NUMBER: PREV200300519820

TITLE: Subcellular localization of SrrAB, a novel two-component regulatory system in *Staphylococcus aureus*.

AUTHOR(S): Pragman, A. A. [Reprint Author]; Schlievert, P. M. [Reprint Author]

CORPORATE SOURCE: University of Minnesota, Minneapolis, MN, USA

SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2003) Vol. 103, pp. B-066.  
<http://www.asmusa.org/mtgsrc/generalmeeting.htm>. cd-rom.  
Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003.  
American Society for Microbiology.  
ISSN: 1060-2011 (ISSN print).

DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 5 Nov 2003  
Last Updated on STN: 5 Nov 2003

AB Background: SrrAB is a novel two-component system that regulates *S. aureus* virulence factors in response to oxygen. SrrA, the putative response regulator, is predicted to encode a DNA-binding protein. SrrB, the putative histidine kinase, is predicted to encode a membrane-spanning protein. We hypothesize that SrrA is localized in the *S. aureus* cytoplasm while SrrB is localized to the membrane. Methods: Polyclonal antibodies were raised against recombinant SrrA as well as the predicted extracellular domain of SrrB by immunizing Dutch Belted Rabbits. *S. aureus* strains DU5875 and DU5875 (pJMY11) were grown microaerobically to post-exponential phase in order to induce maximal expression of SrrAB. Cells were lysed by sonication, and membrane and cytoplasmic extracts of both strains were electrophoresed and blotted by Western analysis with SrrA and SrrB antibodies. *S. aureus* MN8 was immunostained with SrrB or a pre-immune control antibody and visualized by chromogenic peroxidase staining. Results: Both strains DU5875 and DU5875 (pJMY11) demonstrated that SrrA as well as SrrB are localized to the membrane fraction when bacteria are lysed by sonication. SrrA is likely also present in the cytoplasm. Ongoing work will address the localization of SrrAB when other methods are used to lyse the bacteria. *S. aureus* MN8 demonstrated strong chromogenic staining following incubation with SrrB, compared with control antibody. Scanning electron microscopy studies using the SrrB antibody to visualize the membrane distribution of SrrB are

in progress. Conclusion: *S. aureus* SrrB is localized to the bacterial cell membrane. The predicted extracellular domain of SrrB is found on the external cell surface. Sonicated cell extracts indicate that SrrA is also localized to the cell membrane.

L8 ANSWER 18 OF 58 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2003:517239 BIOSIS

DOCUMENT NUMBER: PREV200300519832

TITLE: Two-component gene regulation in the biology of *Enterococcus faecalis*.

AUTHOR(S): Hancock, L. E. [Reprint Author]; Perego, M. [Reprint Author]

CORPORATE SOURCE: Scripps Research Institute, La Jolla, CA, USA

SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2003) Vol. 103, pp. B-078.

<http://www.asmusa.org/mtgsrc/generalmeeting.htm>. cd-rom. Meeting Info.: 103rd American Society for Microbiology General Meeting. Washington, DC, USA. May 18-22, 2003. American Society for Microbiology.

ISSN: 1060-2011 (ISSN print).

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 5 Nov 2003

Last Updated on STN: 5 Nov 2003

AB Enterococci are commensals within the mammalian intestinal tract, but also possess the ability to cause disease in compromised hosts, emerging in recent years as a leading nosocomial pathogen. In association with this emergence has been the acquisition of resistance determinants to multiple antibiotics, making infections caused by these organisms clinically challenging. The ability of these organisms to adapt and respond to different environmental stimuli, including the host environment led us to investigate the role of two-component signal transduction in the regulation of gene expression in *Enterococcus faecalis*. Using a bioinformatic approach we identified 17 two-component systems (TCS), consisting of a sensory histidine kinase and the cognate response regulator, as well as an additional orphan response regulator. In an effort to identify the potential function of each TCS in the biology of *E. faecalis* strain V583, we constructed insertionally inactivated mutations in each of the response regulators. We were unable to inactivate one response regulator. This response regulator shares extensive sequence similarity with the *Bacillus subtilis*, *Staphylococcus aureus*, *Streptococcus pneumoniae* YycF protein, previously shown to be essential for viability in these Gram-positive microorganisms. The biological effect of the remaining mutations was assessed using a number of assays, including antibiotic resistance, biofilm formation, as well as growth under acidic and high salt environments. We identified several TCS related to antibiotic resistance, and found one TCS which controls the initiation of biofilm development by *E. faecalis*.

L8 ANSWER 19 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN

ACCESSION NUMBER: 2002-10378 BIOTECHDS

TITLE: Assay for detecting compounds that modulates histidine kinase activity, by contacting compound with kinase and substrate, and monitoring the rate or absolute amount of phosphate transfer by kinase to the substrate;

plasmid pMal-(RTM)-c2-mediated gene transfer and expression in *Escherichia coli* for drug screening

AUTHOR: GOLDSCHMIDT R; LOELOFF M

PATENT ASSIGNEE: GOLDSCHMIDT R; LOELOFF M

PATENT INFO: US 2002004214 10 Jan 2002

APPLICATION INFO: US 1999-733731 21 Dec 1999

PRIORITY INFO: US 2000-733731 8 Dec 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-171025 [22]

AB DERWENT ABSTRACT:

NOVELTY - Assay for detecting compounds that modulate **histidine kinase** (HK) enzymatic activity or interaction of HK with its cognate response regulator protein, involves contacting a compound (C) with HK and HK substrate, isolating HK substrate by affinity capture and detecting a change in kinase activity by monitoring the rate or absolute amount of phosphate transfer by HK to the substrate in the presence of (C).

DETAILED DESCRIPTION - Assay for detecting compounds that modulate **histidine kinase** (HK) enzymatic activity or interaction of HK with its cognate response regulator protein, involves: (a) identifying compounds that modulate **EspB histidine kinase** enzymatic activity, by admixing a test compound, an **EspB histidine kinase** fusion protein comprising an **EspB histidine kinase** catalytic domain and an affinity capture domain, and a high energy phosphate source, incubating the compound with **histidine kinase** fusion protein and high energy phosphate source, isolating the **EspB histidine kinase** fusion protein by affinity isolation, and detecting a change in kinase activity by monitoring the rate or absolute amount of phosphate transfer to the **EspB histidine kinase** by autophosphorylation in the presence of the compound; or (b) identifying compounds that modulate **histidine kinase** enzymatic activity or modulate interaction of the kinase with its cognate response regulator protein, by admixing a test compound, an **EspA cognate histidine kinase** or its functional derivative, where the kinase has functional **histidine kinase** activity, an **EspA** fusion protein comprising an **EspA** phosphorylation domain and an affinity capture domain, and a high energy phosphate source, incubating the compound with **histidine kinase** or its derivative, the **EspA** fusion protein and the high energy phosphate source, isolating the **EspA** fusion protein by affinity isolation, and detecting a change in kinase activity by monitoring the rate or absolute amount of phosphate transfer by the kinase to the **EspA** fusion protein in the presence of the compound. An INDEPENDENT CLAIM is also included for a **histidine kinase** fusion protein (I) comprising a protein domain of the **espB** gene or its functional derivative having functional catalytic activity and a protein or peptide having at least one affinity capture domain.

WIDER DISCLOSURE - The following are also disclosed as new: (1) construction of **histidine kinase** fusion proteins that maintain catalytic activity, create at least one affinity capture domain and eliminate a hydrophobic membrane-spanning domain contained with the native protein; (2) a cognate response regulator fusion proteins comprising a protein domain of a cognate response regulator that maintains functional transphosphorylation activity, fused to a protein or peptide molecule having affinity capture domain; and (3) **histidine kinase** fusion protein comprising a protein domain or its functional derivative having functional catalytic activity and a protein or peptide having at least one affinity capture domain.

BIOTECHNOLOGY - Preferred Method: The method is conducted in a single scintillant - impregnated or coated vessel. The phosphorylated **EspB histidine kinase** or the **EspA** fusion protein is isolated by affinity capture onto the surface of the vessel. Preferred Protein: The affinity capture protein or peptide is selected from **male** gene of *Escherichia coli*, the glutathione S-transferase encoding gene of *Schistosoma japonicum*, and hexahistidine. The **EspB histidine kinase** catalytic domain comprises the carboxy terminal 311 amino acids of the **espB** gene. The **EspA** cognate **histidine kinase** is **EspB**, its ortholog or a paralog that can transphosphorylate **EspA**. The protein domain of (I) comprises about the

carboxy terminal 397 or 311 amino acids of the espB gene.

ACTIVITY - Antibacterial. No suitable data is given in the source material.

MECHANISM OF ACTION - Modulator of histidine kinase activity (claimed).

USE - The method is useful for detecting modulators of histidine kinase enzyme activity or its interaction with its cognate response regulator protein (claimed). The identified compounds are useful to inhibit growth and kill bacteria that cause infectious disease, while minimizing any potential toxicity.

ADVANTAGE - The method is a robust, sensitive assay of simple design that is easily automated and an assay that can be easily modified to allow different histidine kinase and response regulator targets to be tested without significant modification to the design.

EXAMPLE - To construct affinity capture protein-histidine kinase (MalE-EspB) fusions, pMal-(RTM)-c2 plasmid was used. Two amplifications of espB gene were generated through polymerase chain reaction (PCR) amplification of DNA from *Staphylococcus aureus* strain COL using plaque forming units (Pfu) DNA polymerase and pairs of primers given in the specification. The first amplicon, obtained using primers HKFM02 and HKBM02, encoded the 397 C-terminal amino acids of EspB, starting at Asp212. The two primers had BamHI and HindIII sites, respectively, to allow the cloning into the same sites of the vector maintaining the proper reading frame for the protein fusion. The second amplicon, obtained using primers HKFM03 and HKBM02 encoded the 311 C-terminal amino acids of EspB, starting at Met298. Similar to the first case, the two primers had BamHI and HindIII sites, respectively, to allow the cloning into the same sites of the vector maintaining the proper reading frame for the protein fusion. The maleE-espB fusion gene was transformed into DH5alpha cells for fusion protein expression. One inoculation loop with transformed cells was inoculated into 125 ml of LB medium in the presence of 100 microg/ml of ampicillin. The culture was incubated at 37 degrees C with shaking overnight. The cells were induced for MalE-EspB expression by adding IPTG (isopropyl beta-D-thiogalactopyranoside) to a final concentration of 0.5 mM and incubated with shaking at 37 degrees C. The cells were then harvested after 4 hours of culture. The media was centrifuged and then the pellet was isolated and stored at -80 degrees C for later purification. (17 pages)

L8 ANSWER 20 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN

ACCESSION NUMBER: 2002:359080 SCISEARCH

THE GENUINE ARTICLE: 543NH

TITLE: rgf encodes a novel two-component signal transduction system of *Streptococcus agalactiae*

AUTHOR: Spellerberg B (Reprint); Rozdzinski E; Martin S; Weber-Heynemann J; Lutticken R

CORPORATE SOURCE: Univ Ulm, Dept Med Microbiol & Hyg, Robert Koch Str 8, D-89081 Ulm, Germany (Reprint); Univ Ulm, Dept Med Microbiol & Hyg, D-89081 Ulm, Germany; Univ Hosp Aachen, Inst Med Microbiol, D-52057 Aachen, Germany; Univ Hosp Aachen, Natl Reference Ctr Streptococci, D-52057 Aachen, Germany

COUNTRY OF AUTHOR: Germany

SOURCE: INFECTION AND IMMUNITY, (MAY 2002) Vol. 70, No. 5, pp. 2434-2440.

Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.

ISSN: 0019-9567.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 32

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB The adhesion of gram-positive bacteria to extracellular matrix (ECM) proteins is regarded as an important determinant of pathogenicity. A comparison of the adhesion of *Streptococcus agalactiae* strain O90R to different ECM proteins showed that the most pronounced binding could be observed for immobilized fibrinogen. To investigate the genetic determinants of *S. agalactiae* fibrinogen binding, a pGhost9:ISS1 mutant library was screened for mutants displaying reduced agglutination of fibrinogen-coated latex beads. A putative two-component signal transduction system was identified and designated rgfBDAC. It comprises genes encoding a putative response regulator of 218 amino acids and a putative histidine kinase of 426 amino acids. Comparison of the deduced proteins with the GenBank database revealed a significant similarity to quorum-sensing systems of gram-positive pathogens. Transcription analysis of the rgf locus showed that the encoding genes are located on one transcript. To further characterize the influence of the putative histidine kinase encoded in the rgf locus on the adhesion of *S. agalactiae* to immobilized fibrinogen, a targeted mutant of rgfC was generated. In comparison to the wild-type strain this mutant demonstrated altered fibrinogen binding capacities depending on bacterial cell density. Transcription analysis of secreted and surface-localized *S. agalactiae* proteins in the wild type and the rgfC mutant strain revealed that mRNA levels of the C5a peptidase gene sepB were increased in the mutant strain while the transcription of the secreted CAMP factor gene cfb was unaffected by this mutation. Based on these results, we hypothesize that rgf regulates the expression of bacterial cell surface components.

L8 ANSWER 21 OF 58 SCISEARCH. COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN

ACCESSION NUMBER: 2002:652704 SCISEARCH

THE GENUINE ARTICLE: 579BC

TITLE: Recent progress in *Bacillus subtilis* two-component regulation

AUTHOR: Ogura M; Tanaka T (Reprint)

CORPORATE SOURCE: Tokai Univ, Sch Marine Sci & Technol, Dept Marine Sci, Orido 3-20-1, Shizuoka 4248610, Japan (Reprint); Tokai Univ, Sch Marine Sci & Technol, Dept Marine Sci, Shizuoka 4248610, Japan

COUNTRY OF AUTHOR: Japan

SOURCE: FRONTIERS IN BIOSCIENCE, (AUG 2002) Vol. 7, pp. D1815-D1824.

Publisher: FRONTIERS IN BIOSCIENCE INC, C/O NORTH SHORE UNIV HOSPITAL, BIOMEDICAL RESEARCH CENTER, 350 COMMUNITY DR, MANHASSET, NY 11030 USA.

ISSN: 1093-9946.

DOCUMENT TYPE: General Review; Journal

LANGUAGE: English

REFERENCE COUNT: 77

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Two-component regulatory systems serve to control gene expression in response to environmental and physiological changes. They are widespread among a variety of organisms and most often found in prokaryotes. One of the gram-positive microorganisms *Bacillus subtilis* is a well-studied bacterium whose complete nucleotide sequence has been determined. Thus, it is now possible to study transcription of the whole genome with microarray analysis. In this review we summarize the recent progress in *B. subtilis* two-component regulatory systems by describing the known systems and those for which the function was recently assigned. Also included is an attempt to construct a partial transcriptional network involving several two-component systems. The studies described here are based on the data from traditional genetics and biochemistry, and from microarray analysis of 29 two-component systems.

L8 ANSWER 22 OF 58 MEDLINE on STN DUPLICATE 5  
ACCESSION NUMBER: 2002080831 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11807070  
TITLE: Repression of the *Staphylococcus aureus*  
accessory gene regulator in serum and in vivo.  
AUTHOR: Yarwood Jeremy M; McCormick John K; Paustian Michael L;  
Kapur Vivek; Schlievert Patrick M  
CORPORATE SOURCE: Department of Microbiology, Medical School, University of  
Minnesota, Minneapolis, Minnesota, USA.  
CONTRACT NUMBER: HL36611 (NHLBI)  
SOURCE: Journal of bacteriology, (2002 Feb) 184 (4) 1095-101.  
Journal code: 2985120R. ISSN: 0021-9193.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200203  
ENTRY DATE: Entered STN: 20020128  
Last Updated on STN: 20020320  
Entered Medline: 20020319

AB Subgenomic DNA microarrays were employed to evaluate the expression of the accessory gene regulator (agr locus) as well as multiple virulence-associated genes in *Staphylococcus aureus*. Gene expression was examined during growth of *S. aureus* in vitro in standard laboratory medium and rabbit serum and in vivo in subcutaneous chambers implanted in either nonimmune rabbits or rabbits immunized with staphylococcal enterotoxin B. Expression of RNAIII, the effector molecule of the agr locus, was dramatically repressed in serum and in vivo, despite the increased expression of secreted virulence factors sufficient to cause toxic shock syndrome (TSS) in the animals. Statistical analysis and clustering of virulence genes based on their expression profiles in the various experimental conditions demonstrated no positive correlation between the expression of agr and any staphylococcal virulence factors examined. Disruption of the agr locus had only a minimal effect on the expression in vivo of the virulence factors examined. An effect of immunization on the expression of agr and virulence factors was also observed. These results suggest that agr activation is not necessary for development of staphylococcal TSS and that regulatory circuits responding to the in vivo environment override agr activity.

L8 ANSWER 23 OF 58 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 6  
ACCESSION NUMBER: 2002:267761 BIOSIS  
DOCUMENT NUMBER: PREV200200267761  
TITLE: Histidine kinases as targets for new antimicrobial agents.  
AUTHOR(S): Matsushita, Masayuki [Reprint author]; Janda, Kim D.  
[Reprint author]  
CORPORATE SOURCE: Department of Chemistry, Scripps Research Institute and Skaggs Institute for Chemical Biology, 10550 N. Torrey Pines Road, BCC-582, La Jolla, CA, 92037, USA  
kdjanda@scripps.edu  
SOURCE: Bioorganic and Medicinal Chemistry, (April, 2002) Vol. 10, No. 4, pp. 855-867. print.  
ISSN: 0968-0896.  
DOCUMENT TYPE: Article  
General Review; (Literature Review)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 1 May 2002  
Last Updated on STN: 1 May 2002

AB The emergence and spread of hospital acquired multi drug resistant bacteria present a need for new antibiotics with innovative mode of action. Advances in molecular microbiology and genomics have led to the

identification of numerous bacterial genes coding for proteins that could potentially serve as targets for antibacterial compounds. Histidine kinase promoted two-component systems are extremely common in bacteria and play an important role in essential signal transduction for adapting to bacterial stress. Since signal transduction in mammals occurs by a different mechanism, inhibition of histidine kinases could be a potential target for antimicrobial agents. This review will summarize our current knowledge of the structure and function of histidine kinase and the development of antibiotics with a new mode of action: targeting histidine kinase promoted signal transduction and its subsequent regulation of gene expression system.

L8 ANSWER 24 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN

ACCESSION NUMBER: 2002:756564 SCISEARCH  
THE GENUINE ARTICLE: 591TY

TITLE: Two-component and phosphorelay signal-transduction systems as therapeutic targets

AUTHOR: Stephenson K (Reprint); Hoch J A

CORPORATE SOURCE: Scripps Clin & Res Inst, Dept Mol & Expt Med, MEM-116, 10550 N Torrey Pines Rd, La Jolla, CA 92037 USA (Reprint); Scripps Clin & Res Inst, Dept Mol & Expt Med, La Jolla, CA 92037 USA

COUNTRY OF AUTHOR: USA

SOURCE: CURRENT OPINION IN PHARMACOLOGY, (OCT 2002) Vol. 2, No. 5, pp. 507-512.  
Publisher: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.  
ISSN: 1471-4892.

DOCUMENT TYPE: General Review; Journal  
LANGUAGE: English  
REFERENCE COUNT: 63

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Two-component and phosphorelay signal-transduction systems of pathogenic bacteria control the expression of genes encoding virulence factors and essential functions. Recent systematic gene inactivation studies have confirmed the integral role of two-component systems in the pathogenesis of diseases caused by several microorganisms and highlighted the validity of using these systems as targets for therapeutic intervention. Structural studies of signal-transduction proteins have recently revealed common features that may allow rational drug design for therapeutic intervention. In particular, the conserved domains of response regulators may represent the best targets for inhibition.

L8 ANSWER 25 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:858990 HCAPLUS  
DOCUMENT NUMBER: 138:148485

TITLE: Regulatory relationship of two-component and ABC transport systems and clustering of their genes in the *Bacillus/Clostridium* group, suggest a functional link between them

AUTHOR(S): Joseph, Pascale; Fichant, Gwennaelle; Quentin, Yves; Denizot, Francois

CORPORATE SOURCE: Laboratoire de Chimie Bacterienne, Institut de Biologie Structurale et Microbiologie, CNRS 31, Marseille, 13402, Fr.

SOURCE: Journal of Molecular Microbiology and Biotechnology (2002), 4(5), 503-513  
CODEN: JMMBFF; ISSN: 1464-1801

PUBLISHER: Horizon Scientific Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB On the *Bacillus subtilis* chromosome there are five examples of genes encoding two-component systems with response regulators of the OmpR family adjacent to genes encoding sub-family 9 ABC transport systems. Three of these (yts, yvc, yxd) are very similar in gene organization and in sequence. The authors demonstrate that the TCS and ABC transporter genes do not belong to the same transcriptional unit. The ABC transport and TCS systems are functionally linked, each response regulator controlling the expression of its cognate ABC transporter genes but not its own. Anal. of 48 bacterial genomes revealed that such family clusters only exist in the *Bacillus/Clostridium* group. Evolutionary analyses indicated that almost all clustered OmpR response regulators constitute two groups ("GI" and "GII") whereas almost all clustered sub-family 9 nucleotide-binding domains belong to two other groups ("9A" and "9B"). Interestingly, there is a mutually exclusive clustering between genes encoding "GI" or a "GII" response regulators and genes encoding "9A" or a "9B" nucleotide binding proteins. The authors propose that a two-component system and its cognate ABC transporter genes have evolved as a unit in *Bacillus/Clostridium*, both systems participating in a common physiol. process.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 26 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN  
ACCESSION NUMBER: 2002:602183 SCISEARCH  
THE GENUINE ARTICLE: 571KL  
TITLE: Virulence- and antibiotic resistance-associated  
two-component signal transduction systems of Gram-positive  
pathogenic bacteria as targets for antimicrobial therapy  
Stephenson K; Hoch J A (Reprint)  
AUTHOR:  
CORPORATE SOURCE: Scripps Clin & Res Inst, Dept Mol & Expt Med, Div Cellular  
Biol, MEM-116, 10550 N Torrey Pines Rd, La Jolla, CA 92037  
USA (Reprint); Scripps Clin & Res Inst, Dept Mol & Expt  
Med, Div Cellular Biol, La Jolla, CA 92037 USA  
COUNTRY OF AUTHOR: USA  
SOURCE: PHARMACOLOGY & THERAPEUTICS, (FEB-MAR 2002) Vol. 93, No.  
2-3, pp. 293-305.  
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD,  
LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.  
ISSN: 0163-7258.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 92

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Two-component signal transduction systems are central elements of the virulence and antibiotic resistance responses of opportunistic bacterial pathogens. These systems allow the bacterium to sense and respond to signals emanating from the host environment and to modulate the repertoire of genes expressed to allow invasion and growth in the host. The integral role of two-component systems in virulence and antibiotic sensitivity, and the existence of essential two-component systems in several pathogenic bacteria, suggests that these systems may be novel targets for antimicrobial intervention. This review discusses the potential use of two-component systems as targets for antimicrobial therapy against Gram-positive pathogens and the current status in the development of inhibitors specific for these systems. (C) 2002 Elsevier Science Inc. All rights reserved.

L8 ANSWER 27 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2002:613874 HCAPLUS  
TITLE: Turning virulence on and off in *Staphylococci*  
AUTHOR(S): Muir, Tom W.  
CORPORATE SOURCE: Laboratory of Synthetic Protein Chemistry, Rockefeller  
University, New York City, NY, 10021, USA

SOURCE: Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (2002), BIOL-102. American Chemical Society: Washington, D. C.

CODEN: 69CZPZ

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB The emergence of methicillin-resistant and, more recently, vancomycin-resistant strains of *Staphylococcus aureus* represents an enormous threat to public health. Consequently, there is a pressing need to identify new types of antibacterial agents and it has been suggested that interference with the expression of virulence may represent a promising antibacterial modality. Staphylococcal virulence is regulated by a two-component quorum sensing system, agr, activated by a self-coded autoinducing peptide (AIP). The agr system is widely divergent and is unique in that variant AIPs cross-inhibit agr activation in heterologous combinations. Cross-inhibition, but not self-activation, is widely tolerant of structural diversity in the AIPs so that these two processes must involve different mechanisms of interaction with the resp. receptors. We have used a combination of mol. genetics, protein chemical and chemical synthesis to establish that these AIPs from *S. aureus* contain a thiolactone structure, and that this feature is absolutely necessary for full biol. activity. Moreover, structure-activity studies have allowed key aspects within the AIP and its histidine-kinase receptor, AgrC, involved in the differential activation and inhibition functions to be identified. This has led to the rational design of global inhibitors of virulence within the Staphylococci as well as the development of a model for receptor agonism and antagonism.

L8 ANSWER 28 OF 58 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2001:452628 BIOSIS

DOCUMENT NUMBER: PREV200100452628

TITLE: Histidine kinase of *Staphylococcus aureus*.

AUTHOR(S): Wallis, Nicola Gail [Inventor]; Traini, Christopher Michael [Inventor]; Kosmatka, Anna Lisa [Inventor]; Shilling, Lisa Kathleen [Inventor]; Warren, Richard Lloyd [Inventor]

CORPORATE SOURCE: ASSIGNEE: SmithKline Beecham Corporation, Philadelphia, PA, USA; SmithKline Beecham plc, Boreford, UK

PATENT INFORMATION: US 6270992 August 07, 2001

SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 7, 2001) Vol. 1249, No. 1. e-file. CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English

ENTRY DATE: Entered STN: 26 Sep 2001

Last Updated on STN: 22 Feb 2002

AB The invention provides Histidine kinase polypeptides and polynucleotides encoding Histidine kinase polypeptides and methods for producing such polypeptides by recombinant techniques. Also provided are methods for utilizing Histidine kinase polypeptides to screen for antibacterial compounds.

L8 ANSWER 29 OF 58 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2001:378355 BIOSIS

DOCUMENT NUMBER: PREV200100378355

TITLE: Histidine kinase, 636 HK, of *staphylococcus aureus*.

AUTHOR(S): Burnham, Martin K R [Inventor]; Palmer, Leslie Marie [Inventor]; Throup, John Peter [Inventor, Reprint author];

Van Horn, Stephanie [Inventor]; Warren, Richard Lloyd [Inventor]

CORPORATE SOURCE: Royersford, PA, USA

ASSIGNEE: SmithKline Beecham Corporation

PATENT INFORMATION: US 6194174 February 27, 2001

SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 27, 2001) Vol. 1243, No. 4. e-file.

CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English

ENTRY DATE: Entered STN: 8 Aug 2001  
Last Updated on STN: 19 Feb 2002

AB The invention provides 636 HK polypeptides and polynucleotides encoding 636 HK polypeptides and methods for producing such polypeptides by recombinant techniques. Also provided are methods for utilizing 636 HK polypeptides to screen for antibacterial compounds.

L8 ANSWER 30 OF 58 MEDLINE on STN

ACCESSION NUMBER: 2001469003 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11513618

TITLE: The *srhSR* gene pair from *Staphylococcus aureus*: genomic and proteomic approaches to the identification and characterization of gene function.

AUTHOR: Throup J P; Zappacosta F; Lunsford R D; Annan R S; Carr S A; Lonsdale J T; Bryant A P; McDevitt D; Rosenberg M; Burnham M K

CORPORATE SOURCE: Anti-infectives Research, GlaxoSmithKline Pharmaceuticals Research and Development, Collegeville, Pennsylvania 19426, USA.. John\_Throup-1@sbphrd.com

SOURCE: Biochemistry, (2001 Aug 28) 40 (34) 10392-401.  
Journal code: 0370623. ISSN: 0006-2960.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200109

ENTRY DATE: Entered STN: 20010830  
Last Updated on STN: 20030325  
Entered Medline: 20010927

AB Systematic analysis of the entire two-component signal transduction system (TCSTS) gene complement of *Staphylococcus aureus* revealed the presence of a putative TCSTS (designated *SrhSR*) which shares considerable homology with the *ResDE* His-Asp phospho-relay pair of *Bacillus subtilis*. Disruption of the *srhSR* gene pair resulted in a dramatic reduction in growth of the *srhSR* mutant, when cultured under anaerobic conditions, and a 3-log attenuation in growth when analyzed in the murine pyelonephritis model. To further understand the role of *SrhSR*, differential display two-dimensional gel electrophoresis was used to analyze the cell-free extracts derived from the *srhSR* mutant and the corresponding wild type. Proteins shown to be differentially regulated were identified by mass spectrometry in combination with protein database searching. An *srhSR* deletion led to changes in the expression of proteins involved in energy metabolism and other metabolic processes including arginine catabolism, xanthine catabolism, and cell morphology. The impaired growth of the mutant under anaerobic conditions and the dramatic changes in proteins involved in energy metabolism shed light on the mechanisms used by *S. aureus* to grow anaerobically and indicate that the staphylococcal *SrhSR* system plays an important role in the regulation of energy transduction in response to changes in oxygen availability. The combination of proteomics, bio-informatics, and microbial genetics employed here represents a powerful set of techniques which can be applied to the study of bacterial gene function.

ACCESSION NUMBER: 2001337274 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11136460  
TITLE: Group A streptococcal growth phase-associated virulence factor regulation by a novel operon (Fas) with homologies to two-component-type regulators requires a small RNA molecule.  
AUTHOR: Kreikemeyer B; Boyle M D; Buttaro B A; Heinemann M; Podbielski A  
CORPORATE SOURCE: Department of Medical Microbiology and Hygiene, University Hospital Ulm, Robert-Koch-Str. 8, D-89081 Ulm, Germany.  
SOURCE: Molecular microbiology, (2001 Jan) 39 (2) 392-406.  
Journal code: 8712028. ISSN: 0950-382X.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200106  
ENTRY DATE: Entered STN: 20010618  
Last Updated on STN: 20010618  
Entered Medline: 20010614

AB A novel growth phase-associated two-component-type regulator, Fas (fibronectin/fibrinogen binding/haemolytic activity/streptokinase regulator), of *Streptococcus pyogenes* was identified in the M1 genome sequence, based on homologies to the histidine protein kinase (HPK) and response regulator (RR) part of the *Staphylococcus aureus* Agr and *Streptococcus pneumoniae* Com quorum-sensing systems. The fas operon, present in all 12 tested M serotypes, was transcribed as polycystronic message (fasBCA) and contained genes encoding two potential HPKs (FasB and FasC) and one RR (FasA). Downstream of fasBCA, we identified a small 300 nucleotide monocistronic transcript, designated fasX, that did not appear to encode true peptide sequences. Measurements of luciferase promoter fusions revealed a growth phase-associated transcription of fasBCA and fasX, with peak activities during the late exponential phase. Insertional mutagenesis disrupting fasBCA and fasA led to a phenotype similar to agr-null mutations in *S. aureus*, with prolonged expression of extracellular matrix protein-binding adhesins and reduced expression of secreted virulence factors such as streptokinase and streptolysin S. In addition, fasX transcription was dependent on the RR FasA; however, deletion mutagenesis of fasX resulted in a similar phenotype to that of the fasBCA or fasA mutants. Complementation of the fasX deletion mutant, with the fasX gene expressed in trans from a plasmid, restored the wild-type fasBCA regulation pattern. This strongly suggested that fasX, a putative non-translated RNA, is the main effector molecule of the fas regulon. However, using spent culture supernatants from wild-type and fas mutant strains, we were not able to show an influence on the logarithmic growth phase expression of fas and dependent genes. Thus, despite structural and functional similarities between fas and agr, to date the fas operon appears not to be involved in group A streptococcal (GAS) quorum-sensing regulation.

L8 ANSWER 32 OF 58 HCPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2001:455510 HCPLUS  
DOCUMENT NUMBER: 135:192773  
TITLE: Characterization of bacteriocin N15 produced by *Enterococcus faecium* N15 and cloning of the related genes  
AUTHOR(S): Losteinkit, Chanvadee; Uchiyama, Keiji; Ochi, Shuichiro; Takaoka, Tomoyo; Nagahisa, Keisuke; Shioya, Suteaki  
CORPORATE SOURCE: Department of Biotechnology, Graduate School of Engineering, Osaka University, Suita, 565-0871, Japan  
SOURCE: Journal of Bioscience and Bioengineering (2001), 91(4), 390-395

CODEN: JBBIF6; ISSN: 1389-1723

PUBLISHER: Society for Bioscience and Bioengineering, Japan  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Enterococcus faecium N15 was isolated from nuka (Japanese rice-bran paste), which is utilized as starter in the fermenting of vegetables, and was found to produce a bacteriocin that exhibited a broad spectrum of activity, including activity against Listeria monocytogenes and Bacillus circulans JCM2504. The bacteriocin was sensitive to proteases ( $\alpha$ -chymotrypsin, proteinase K, trypsin, and pepsin) and  $\alpha$ -amylase, but it was resistant to lipase. The bacteriocin was resistant to heat treatment at 100°C for 2 h, but its activity was completely lost after autoclaving at 121°C for 15 min. It was active over a wide pH range from 2.0 to 10.0. The bacteriocin showed bactericidal activity against Lactobacillus sake JCM1157 at a concentration of

40

AU/mL. Its mol. weight was estimated by SDS-PAGE to be about 3-5 kDa. PCR primers were designed based on the conserved amino acid sequences of class IIa bacteriocins. A 3-kb DNA fragment was amplified and three open reading frames (ORFs) were found. The first encodes a probable immunity protein of 103 amino acid residues and shows complete homol. with the putative immunity protein of E. faecium DPC1146. The second and third ORFs resp. encode a probable transposase gene and an inducing factor. The upstream region of the immunity gene, in which the bacteriocin structural gene is located, was amplified. A homol. search revealed that the bacteriocin produced by E. faecium N15 exhibits complete identity to enterocin A, a bacteriocin produced by E. faecium DPC1146. PCR using the primers designed in this study is a rapid and sufficient method of screening for bacteriocin-producing strains.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 33 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
DUPLICATE 7

ACCESSION NUMBER: 2001-03236 BIOTECHDS

TITLE: Histidine-kinase polypeptides and polynucleotides, useful for treating bacterial infections caused by *Staphylococcus aureus* such as otitis media, thyroiditis, empyema and for screening antibacterial compounds;  
the use of recombinant histidine-kinase

AUTHOR: Throup J P; Palmer L M; Burnham M K; Warren R L; van Horn S

PATENT ASSIGNEE: SK-Beecham

LOCATION: Philadelphia, PA, USA; Brentford, UK.

PATENT INFO: WO 2000068360 16 Nov 2000

APPLICATION INFO: WO 2000-US12862 11 May 2000

PRIORITY INFO: US 1999-310275 12 May 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2001-016089 [02]

AB An isolated histidine-kinase (636HK) protein (I) is claimed. (I) contains a sequence having at least 95% identity to a fully defined sequence (S1) of 608 amino acids over its entire length, a sequence containing S1, or a sequence encoded by a recombinant polynucleotide with a fully defined sequence of 1,827 bp. Also claimed are: an isolated polynucleotide (II); diagnosing or prognosing a disease or a susceptibility to a disease in an individual related to expression or activity of (I); production of (I); producing a host cell by an expression system or its membrane expressing (I); a host cell or a membrane expressing (I); an antibody immunospecific for (I); screening to identify compounds that agonize or inhibit the function (I); and an agonist or antagonist to (I). (I) is useful to treat an individual in need of enhanced activity

or expression of or immunological response to (I). The antagonists or agonists of (I) are useful for treating microbial infections. (I) and (II) are useful as research reagent material for discovery of treatment and diagnosis. (I), (II) and agonists and antagonists are useful in treatment of *Helicobacter pylori* infection, etc. (40pp)

L8 ANSWER 34 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
DUPLICATE 8

ACCESSION NUMBER: 2001-00945 BIOTECHDS

TITLE: *Histidine-kinase family polypeptides obtained from *Staphylococcus aureus*, useful for developing antibacterial compounds; vector-mediated gene transfer and expression in host cell, antibody, agonist and antagonist, appl. cancer and bacterium infection therapy*

AUTHOR: Wallis N G

PATENT ASSIGNEE: SK-Beecham

LOCATION: Philadelphia, PA, USA.

PATENT INFO: WO 2000056865 28 Sep 2000

APPLICATION INFO: WO 2000-US6206 9 Mar 2000

PRIORITY INFO: US 1999-274058 22 Mar 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2000-638259 [61]

AB A *histidine-kinase* family protein containing a sequence that is or has at least 95% identity to a sequence of 346 amino acids, or a protein encoded by nucleotides 222-1,258 of a 1,500 bp sequence, is new. Also claimed are: a polynucleotide encoding the protein expressed by *histidine-kinase* gene contained in *Staphylococcus aureus*; diagnosing or prognosing a disease or susceptibility to a disease in an individual related to expression or activity of the protein; production of the protein; producing a host cell containing an expression system, or membrane, by transforming or transfecting a cell with an expression system containing the polynucleotide; a host cell; an antibody; screening to identify compounds that agonize or antagonize protein function; and an agonist or antagonist. The protein, polynucleotide and agonists or antagonists are useful for treating an individual in need of enhanced activity, expression or immunological response to the protein. The protein and its agonist or antagonist are useful for treating bacterial infections, which in turn is useful in treating bacterial induced cancers, ulcers and gastritis. (39pp)

L8 ANSWER 35 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
DUPLICATE 9

ACCESSION NUMBER: 2001-00532 BIOTECHDS

TITLE: *New histidine-kinase polypeptide and polynucleotide, useful for treating, preventing or diagnosing microbial diseases, especially infections caused by *Staphylococcus aureus*, e.g. 'otitis media, thyroiditis or wound infection; vector-mediated gene transfer and expression in host cell, antibody, agonist and antagonist*

AUTHOR: Wallis N G

PATENT ASSIGNEE: SK-Beecham

LOCATION: Philadelphia, PA, USA.

PATENT INFO: WO 2000056154 28 Sep 2000

APPLICATION INFO: WO 2000-US6133 8 Mar 2000

PRIORITY INFO: US 1999-272414 19 Mar 1999

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2000-611569 [58]

AB A *Staphylococcus aureus* WCUH-29 (NCIMB 40771) histidine-kinase (hk-I) protein containing a 583 amino acid sequence, a sequence with at least 95% identity or a sequence encoded by a recombinant polynucleotide containing nucleotides 87-1,835 bp of a 2,244 bp sequence, is new. Also claimed are: treating an individual in need of enhanced or inhibited activity or expression of hk-I; diagnosing or prognosing a disease or susceptibility to a disease related to expression or activity of hk-I in an individual; producing hk-I; producing a host cell containing an expression system or membrane expressing hk-I; a host cell or a membrane expressing hk-I; an antibody; screening or identifying compounds that agonize or inhibit the function of hk-I; and an agonist or antagonist of hk-I. The protein and polynucleotide are useful for treating, preventing or diagnosing microbial diseases, especially infections caused by *Staphylococcus aureus*. These diseases include otitis, media, thyroiditis, cerebral abscess, toxic shock syndrome, etc. (39pp)

L8 ANSWER 36 OF 58 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2001:239703 BIOSIS

DOCUMENT NUMBER: PREV200100239703

TITLE: Sensor histidine kinase of *Staphylococcus Aureus*.

AUTHOR(S): Wallis, Nicola Gail [Inventor]

CORPORATE SOURCE: ASSIGNEE: SmithKline Beecham Corporation

PATENT INFORMATION: US 6127147 October 03, 2000

SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 3, 2000) Vol. 1239, No. 1. e-file.

CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English

ENTRY DATE: Entered STN: 16 May 2001

Last Updated on STN: 18 Feb 2002

AB The invention provides histidine kinase polypeptides and DNA (RNA) encoding histidine kinase polypeptides and methods for producing such polypeptides by recombinant techniques. Also provided are methods for utilizing histidine kinase polypeptides to screen for antibacterial compounds.

L8 ANSWER 37 OF 58 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2001:70585 BIOSIS

DOCUMENT NUMBER: PREV200100070585

TITLE: Sensor histidine kinase of *Staphylococcus aureus*.

AUTHOR(S): Wallis, Nicola Gail [Inventor]

CORPORATE SOURCE: ASSIGNEE: SmithKline Beecham Corporation; SmithKline Beecham, p.l.c., UK

PATENT INFORMATION: US 6071894 June 06, 2000

SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (June 6, 2000) Vol. 1235, No. 1. e-file.

CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English

ENTRY DATE: Entered STN: 7 Feb 2001

Last Updated on STN: 12 Feb 2002

AB The invention provides Histidine Kinase polypeptides and polynucleotides encoding Histidine Kinase polypeptides and methods for producing such polypeptides by recombinant techniques. Also provided are methods for utilizing Histidine Kinase polypeptides or polynucleotides to screen for antibacterial compounds.

L8 ANSWER 38 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2000:814336 HCAPLUS  
 DOCUMENT NUMBER: 133:359212  
 TITLE: **Staphylococcus aureus**  
 two-component signal transduction **histidine kinase**-related 509HK proteins and polynucleotides for screening of antibacterial agents  
 INVENTOR(S): Bae, Weonhye; Van Horn, Stephanie; Warren, Richard L.; Biswas, Sanjoy; Throup, John P.; Burnham, Martin K. R.  
 PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; SmithKline Beecham PLC  
 SOURCE: PCT Int. Appl., 37 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000067783	A1	20001116	WO 2000-US11917	20000503
W: JP RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6406889	B1	20020618	US 2000-564954	20000504
PRIORITY APPLN. INFO.:			US 1999-132935P	P 19990506
AB	The invention provides <i>S. aureus</i> 509HK polypeptides and polynucleotides encoding 509HK polypeptides and methods for producing such polypeptides by recombinant techniques. Also provided are methods for utilizing 509HK polypeptides to screen for antibacterial compds.			
REFERENCE COUNT:	2	THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

L8 ANSWER 39 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2000:814249 HCAPLUS  
 DOCUMENT NUMBER: 133:359809  
 TITLE: **Cloning, sequencing and expression of Staphylococcus aureus histidine kinase 0623HK and its therapeutic applications**  
 INVENTOR(S): Bae, Weonhye; Van Horn, Stephanie; Warren, Richard L.; Biswas, Sanjoy; Throup, John P.; Burnham, Martin K. R.  
 PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; SmithKline Beecham PLC  
 SOURCE: PCT Int. Appl., 40 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000067575	A1	20001116	WO 2000-US12046	20000503
W: JP RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			US 1999-132759P	P 19990506
AB	The invention provides <b>histidine kinase</b> 0623HK and DNA sequences encoding 0623HK and methods for producing 0623HK by recombinant techniques. Also provided are methods for utilizing 0623HK to screen for antibacterial compds. In a further aspect, the invention relates to the uses of 0623HK in diagnostic assays for detecting diseases associated with microbial infections and conditions associated with			

such infections. The 0623HK has protein sequence homol. with YesM polypeptide that may be a member of a two-component signal transduction histidine kinase family.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 40 OF 58 MEDLINE on STN DUPLICATE 10  
ACCESSION NUMBER: 2001284536 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11087872  
TITLE: Rational design of a global inhibitor of the virulence response in *Staphylococcus aureus*, based in part on localization of the site of inhibition to the receptor-histidine kinase, AgrC.  
AUTHOR: Lyon G J; Mayville P; Muir T W; Novick R P  
CORPORATE SOURCE: Laboratory of Synthetic Protein Chemistry, The Rockefeller University, 1230 York Avenue, New York, NY 10021, USA.  
CONTRACT NUMBER: AI 42783 (NIAID)  
GM07739 (NIGMS)  
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2000 Nov 21) 97 (24) 13330-5.  
Journal code: 7505876. ISSN: 0027-8424.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200105  
ENTRY DATE: Entered STN: 20010529  
Last Updated on STN: 20010529  
Entered Medline: 20010524

AB Two-component signaling systems involving receptor-histidine kinases are ubiquitous in bacteria and have been found in yeast and plants. These systems provide the major means by which bacteria communicate with each other and the outside world. Remarkably, very little is known concerning the extracellular ligands that presumably bind to receptor-histidine kinases to initiate signaling. The two-component agr signaling circuit in *Staphylococcus aureus* is one system where the ligands are known in chemical detail, thus opening the door for detailed structure-activity relationship studies. These ligands are short (8- to 9-aa) peptides containing a thiolactone structure, in which the alpha-carboxyl group of the C-terminal amino acid is linked to the sulfhydryl group of a cysteine, which is always the fifth amino acid from the C terminus of the peptide. One unique aspect of the agr system is that peptides that activate virulence expression in one group of *S. aureus* strains also inhibit virulence expression in other groups of *S. aureus* strains. Herein, it is demonstrated by switching the receptor-histidine kinase, AgrC, between strains of different agr specificity types, that intragroup activation and intergroup inhibition are both mediated by the same group-specific receptors. These results have facilitated the development of a global inhibitor of virulence in *S. aureus*, which consists of a truncated version of one of the naturally occurring thiolactone peptides.

L8 ANSWER 41 OF 58 MEDLINE on STN DUPLICATE 11  
ACCESSION NUMBER: 2000100755 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10633099  
TITLE: Expression of the multidrug resistance transporter NorA from *Staphylococcus aureus* is modified by a two-component regulatory system.  
AUTHOR: Fournier B; Aras R; Hooper D C  
CORPORATE SOURCE: Infectious Disease Division and Medical Services, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts 02114-2696, USA.

CONTRACT NUMBER: AI23988 (NIAID)  
SOURCE: Journal of bacteriology, (2000 Feb) 182 (3) 664-71.  
Journal code: 2985120R. ISSN: 0021-9193.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200002  
ENTRY DATE: Entered STN: 20000218  
Last Updated on STN: 20000218  
Entered Medline: 20000210

AB To dissect genetically the regulation of *NorA*, a multidrug transporter of *Staphylococcus aureus*, we analyzed the differential expression of the *norA* promoter using a transcriptional fusion with a beta-lactamase reporter gene. Expression studies with an *arlS* mutant revealed that the *norA* promoter is *ArLS* dependent. The *arlR-arlS* locus was shown to code for a two-component regulatory system. The protein *ArLR* has strong similarity to response regulators, and *ArLS* has strong similarity to protein histidine kinases. We have also analyzed the 350-bp region upstream of the Shine-Dalgarno sequence of *norA* by gel mobility shift experiments. It was shown that only the 115-bp region upstream of the promoter was necessary for multiple binding of an 18-kDa protein. From transcriptional fusions, we have localized four different putative boxes of 6 bp, which appear to play a role in the binding of the 18-kDa protein and in the up-regulation of *norA* expression in the presence of the *arlS* mutation. Furthermore, the gel mobility shift of the 18-kDa protein was modified in the presence of the *arlS* mutation, and the *arlS* mutation altered the growth-phase regulation of *NorA*. These results indicate that expression of *norA* is modified by a two-component regulatory system.

L8 ANSWER 42 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN  
ACCESSION NUMBER: 2000:147405 SCISEARCH  
THE GENUINE ARTICLE: 285BF  
TITLE: A genomic analysis of two-component signal transduction in *Streptococcus pneumoniae*  
AUTHOR: Throup J P; Koretke K K; Bryant A P; Ingraham K A; Chalker A F; Ge Y G; Marra A; Wallis N G; Brown J R; Holmes D J; Rosenberg M; Burnham M K R (Reprint)  
CORPORATE SOURCE: SMITHKLINE BEECHAM PHARMACEUT RES & DEV, ANTIINFECT RES, 1250 S COLLEGEVILLE RD, COLLEGEVILLE, PA 19426 (Reprint); SMITHKLINE BEECHAM PHARMACEUT RES & DEV, ANTIINFECT RES, COLLEGEVILLE, PA 19426; SMITHKLINE BEECHAM PHARMACEUT RES & DEV, BIOINFORMAT, COLLEGEVILLE, PA 19426  
COUNTRY OF AUTHOR: USA  
SOURCE: MOLECULAR MICROBIOLOGY, (FEB 2000) Vol. 35, No. 3, pp. 566-576.  
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND.  
ISSN: 0950-382X.  
DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE  
LANGUAGE: English  
REFERENCE COUNT: 44

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB A genomics-based approach was used to identify the entire gene complement of putative two-component signal transduction systems (TCSTSs) in *Streptococcus pneumoniae*. A total of 14 open reading frames (ORFs) were identified as putative response regulators, 13 of which were adjacent to genes encoding probable histidine kinases. Both the histidine kinase and response regulator proteins were categorized into subfamilies on the basis of phylogeny. Through a systematic programme of mutagenesis, the importance of each novel TCSTS

was determined with respect to viability and pathogenicity. One TCSTS was identified that was essential for the growth of *S. pneumoniae*. This locus was highly homologous to the *ycfFG* gene pair encoding the essential response regulator/histidine kinase proteins identified in *Bacillus subtilis* and *Staphylococcus aureus*. Separate deletions of eight other loci led in each case to a dramatic attenuation of growth in a mouse respiratory tract infection model, suggesting that these signal transduction systems are important for the *in vivo* adaptation and pathogenesis of *S. pneumoniae*. The identification of conserved TCSTSs important for both pathogenicity and viability in a Gram-positive pathogen highlights the potential of two-component signal transduction as a multicomponent target for antibacterial drug discovery.

L8 ANSWER 43 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:156175 HCAPLUS

DOCUMENT NUMBER: 133:115743

TITLE: Identification of the Up- and Down-Regulated Genes in Vancomycin-Resistant *Staphylococcus aureus* Strains Mu3 and Mu50 by cDNA Differential Hybridization Method

AUTHOR(S): Kuroda, Makoto; Kuwahara-Arai, Kyoko; Hiramatsu, Keiichi

CORPORATE SOURCE: Department of Bacteriology, Faculty of Medicine, Juntendo University, Bunkyo-ku, Tokyo, 113-8421, Japan

SOURCE: Biochemical and Biophysical Research Communications (2000), 269(2), 485-490

CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We previously reported the first vancomycin-resistant *Staphylococcus aureus* (VRSA) clin. strain, Mu50, whose cell wall is remarkably thickened resulting from the activation of cell-wall synthesis. To explore the genetic basis for the vancomycin resistance, cDNA differential hybridization was performed using RNAs extracted from a set of closely related *S. aureus* strains with various levels of vancomycin susceptibilities. The strains were Mu3 (MIC = 2 µg/mL), Mu50 (MIC = 8 µg/mL), and a susceptible revertant of Mu50, Mu50ω (MIC = 0.5 µg/mL). In this study, we report identification of a novel response regulator, designated vraR (standing for vancomycin-resistance associated gene R) whose transcription was remarkably up-regulated in Mu3 and Mu50 as compared to Mu50ω. Exptl. over-expression of VraR in vancomycin-susceptible strain N315P raised vancomycin resistance of the strain. Also, the genes coding for fructose utilization, fatty acid metabolism, and two putative ATP-binding cassette (ABC) transporter genes were found to be up-regulated in Mu3 and Mu50. On the other hand, Protein A expression was suppressed in Mu50, as compared with Mu3 and Mu50ω. We consider that the response regulator vraR is one of the key regulators modulating the level of vancomycin-resistance in *S. aureus*. Presumed increased uptake of fructose and altered fatty acid metabolism may also contribute to vancomycin resistance by supplying more precursor metabolites for cell-wall synthesis. (c) 2000 Academic Press.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 44 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
DUPLICATE 12

ACCESSION NUMBER: 1999-12556 BIOTECHDS

TITLE: Novel histidine-kinase polynucleotides and polypeptides used to screen for antibacterial compounds; recombinant histidine-kinase, nucleic acid, antibody and antagonist used in disease diagnosis, therapy, gene therapy and nucleic acid vaccine

AUTHOR: Wallis N G; Shilling L K; Mooney J L; Debouck C; Zhong Y; Jaworski D D; Wang M; Throup J P

PATENT ASSIGNEE: SK-Beecham

LOCATION: Philadelphia, PA, USA.

PATENT INFO: WO 9936508 22 Jul 1999

APPLICATION INFO: WO 1999-US610 12 Jan 1999

PRIORITY INFO: US 1998-6627 13 Jan 1998

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 1999-444390 [37]

AB A *Staphylococcus aureus histidine-kinase* (HK) nucleic acid (NA, I) and protein are claimed. (I)

has a given 2,201 bp DNA sequence, is at least 70% identical to a NA that encodes a given 451 amino acid protein sequence, or encodes a protein at least 70% identical to that sequence. Also claimed is a NA at least 70% identical to a NA encoding a mature HK derived from *S. aureus*. Also covered are: a vector encoding (I); a host cell transformed by that vector; a means of producing HK by culturing that cell; an antibody specific to HK; an antagonist (A) that inhibits HK **expression** or activity; a means of treating disease using the HK or (A); a means of diagnosing disease related to HK **expression**; a means of identifying compounds that modify HK activity; a means of inducing an immune response using the HK or a vector encoding it; a NA at least 70% identical to a NA encoding a 219 amino acid protein sequence; a NA at least 70% identical to a 2,201 or 736 bp DNA sequence; a HK with a 451 amino acid protein sequence; and a protein at least 70% identical to that sequence. These can be used in disease diagnosis, therapy, drug screening, gene therapy and in a nucleic acid vaccine. (43pp)

L8 ANSWER 45 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
DUPLICATE 13

ACCESSION NUMBER: 1999-08025 BIOTECHDS

TITLE: New *Staphylococcus aureus histidine-kinase* (HK) polypeptide and polynucleotides, useful for screening for antibiotics and for diagnosis, prevention and treatment of *Staphylococci* infections;

recombinant enzyme production via vector-mediated gene transfer and **expression** in a bacterium, antisense, antibody and antagonist for gene therapy and nucleic acid vaccine

AUTHOR: Traini C M; Kosmatka A L; Shilling L K; Warren R L; Wallis N G

PATENT ASSIGNEE: SK-Beecham

LOCATION: Philadelphia, PA, USA; Brentford, UK.

PATENT INFO: EP 911406 28 Apr 1999

APPLICATION INFO: EP 1998-305806 21 Jul 1998

PRIORITY INFO: US 1997-963901 4 Nov 1997; US 1997-54073 29 Jul 1997

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 1999-246418 [21]

AB A *Staphylococcus aureus histidine-kinase* (HK) (I), which is part of the 2 component signal

transduction system and at least 70% identical to a fully defined 147 amino acid protein sequence, is new. Also claimed are: a polynucleotide (II) (DNA or RNA), which is at least 70% identical to (I) or the mature HK protein **expressed** in *S. aureus* WCUH-29 (NCIMB 40771); a vector containing (II); a host cell containing the vector; an antibody immunospecific for (I); an antagonist which inhibits the activity or **expression** of (I); and the production of (I). (I) and (II) may be useful for the diagnosis of the stage and type of infection caused by an organism with the HK gene and for the screening of compounds which affect the activity of the protein. Antagonists, i.e. antibacterial drugs, may be used to inhibit HK activity and agonists to enhance HK

activity. The products may also be used for gene therapy with antisense sequences and nucleic acid vaccines. The antibodies produced may be used for immunization to prevent disease. (39pp)

L8 ANSWER 46 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 1999:421810 HCAPLUS  
DOCUMENT NUMBER: 131:69294  
TITLE: *Staphylococcus histidine protein kinase gene espB and response regulator gene espA and methods for screening for antibacterial agents and for treating bacterial infections*  
INVENTOR(S): Benton, Bret; Malouin, Francois; Martin, Patrick K.; Schmid, Molly B.; Sun, Dongxu  
PATENT ASSIGNEE(S): Microcide Pharmaceuticals, Inc., USA  
SOURCE: PCT Int. Appl., 108 pp.  
CODEN: PIIXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932657	A1	19990701	WO 1997-US23912	19971223
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9859033	A1	19990712	AU 1998-59033	19971223
US 6514746	B1	20030204	US 1998-82077	19980520
PRIORITY APPLN. INFO.:			US 1995-3798P	P 19950915
			US 1995-9102P	P 19951222
			US 1996-713718	A2 19960913
			WO 1997-US23912	A 19971223

AB This disclosure describes isolated or purified DNA sequences, useful for the development of antibacterial agents, which contain the coding sequences of bacterial genes which encode the components of a two-component regulatory pair. It further describes isolated or purified DNA sequences which are portions of such bacterial genes, which are useful as probes to identify the presence of the corresponding gene or the presence of a bacteria containing that gene. Also described are hypersensitive mutant cells containing a mutant gene corresponding to any of the identified sequences and methods of screening for antibacterial agents using such hypersensitive cells. In addition it describes methods of treating bacterial infections by administering an antibacterial agent active against one of the identified targets, as well as pharmaceutical compns. effective in such treatments. The espAB operon of *S. aureus* was cloned and sequenced. Sequence homologies indicate that these two genes encode a histidine protein kinase-response regulator pair. A method for screening substances which inhibit the EspAB system is presented. This method comprises a wild-type *S. aureus* strain and a mutant *S. aureus* strain which has a temperature-sensitive mutation in the espAB operon. Since the espAB operon is essential for *S. aureus* growth, inhibitors of the mutant are potential antibacterial agents.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 47 OF 58 HCAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 1999:219876 HCAPLUS  
DOCUMENT NUMBER: 130:247875

TITLE: Polynucleotide and polypeptide sequences from  
*Staphylococcus aureus*  
expressed in infected tissue

INVENTOR(S): Lonetto, Michael Arthur; Warren, Patrick Vernon;  
Burnham, Martin Karl Russel

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Smithkline  
Beecham Plc

SOURCE: Eur. Pat. Appl., 70 pp.  
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 905243	A2	19990331	EP 1998-306185	19980803
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2239817	AA	19990205	CA 1998-2239817	19980805
JP 11155586	A2	19990615	JP 1998-255927	19980805

PRIORITY APPLN. INFO.: US 1997-55387P P 19970805

AB The invention provides novel polypeptides and polynucleotides encoding such polypeptides from *Staphylococcus aureus* and methods for producing such polypeptides by recombinant techniques. Thus, 14 partial or full-length gene sequences and the deduced amino acid sequences of their encoded proteins are provided. Also provided are methods for utilizing such polypeptides to screen for antibacterial compds.

L8 ANSWER 48 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
DUPLICATE 14

ACCESSION NUMBER: 1998-11158 BIOTECHDS

TITLE: DNA encoding staphylococcal histidine-kinase;

*Staphylococcus aureus*  
recombinant protein preparation, DNA probe, and antagonist, used as antibiotic or for infectious disease therapy, gene therapy or nucleic acid vaccine, etc.

AUTHOR: Wallis N G

PATENT ASSIGNEE: SK-Beecham

LOCATION: Philadelphia, PA, USA; Brentford, UK.

PATENT INFO: EP 870831 14 Oct 1998

APPLICATION INFO: EP 1998-302776 8 Apr 1998

PRIORITY INFO: US 1997-43489 10 Apr 1997

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 1998-523158 [45]

AB A new DNA sequence has at least 70% identity to a DNA sequence encoding a specified 363 amino acid protein sequence. Also claimed are: cDNA and DNA with at least 15 contiguous nucleotides of the new sequence (DNA probe); a *Staphylococcus aureus* WCUH 29 (NCIMB 40771) DNA sequence encoding histidine-kinase; a vector containing the DNA; a host cell containing the vector; producing the protein using the host cell; an antibody against the protein; and an antagonist which inhibits activity of the protein. The DNA and protein may be used for infectious disease diagnosis, therapy or gene therapy, in a recombinant vaccine or a nucleic acid vaccine, or for drug screening. Diseases associated with expression of the protein include otitis media, empyema, infective endocarditis, secretory diarrhea, cerebral abscess, blepharitis, perinephric abscess, impetigo or osteomyelitis, etc. Antibodies may be used as antibiotics. (30pp)

L8 ANSWER 49 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN

DUPPLICATE 15

ACCESSION NUMBER: 1998-10739 BIOTECHDS

TITLE: New DNA encoding *Staphylococcus aureus* histidine-kinase used to prevent, treat, diagnose and vaccinate;

against respiratory tract infection, cardiac, gastrointestinal, central nervous system, eye, kidney, urinary tract, skin, bone and joint disorder

AUTHOR: Wallis N G

PATENT ASSIGNEE: SK-Beecham

LOCATION: Philadelphia, PA, USA; Brentford, UK.

PATENT INFO: EP 863208 9 Sep 1998

APPLICATION INFO: EP 1998-301167 17 Feb 1998

PRIORITY INFO: US 1997-39478 25 Feb 1997

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 1998-458839 [40]

AB An isolated 2,700 bp nucleic acid (A) with at least 70% identity to a nucleic acid encoding an 861 amino acid protein (B), of given sequence, is claimed. Also claimed are nucleic acids complementary to (A), and partial sequences of (A). (A) encodes the mature histidine-kinase protein expressed by the gene NCIMB 40771. The claims also cover a vector containing (A), and a host cell transformed by that vector. Also covered are: the protein (B), a protein at least 70% identical to (B), an antibody (Ab) specific to (B), and an antagonist that inhibits (B)'s activity. The claims extend to a nucleic acid that can be obtained by screening a library containing a complete (A) under stringent conditions, and using a DNA probe with at least a partial sequence of (A). This is of use in treating an individual in need of histidine-kinase. Either the protein, or the DNA encoding it can be delivered. Alternatively the antagonist of (B) can be used to inhibit histidine-kinase. (A) can also be used to diagnose diseases related to (B) expression. (B) can be used to induce an immune response, causing production of (B)-Ab. (31pp)

L8 ANSWER 50 OF 58 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
DUPLICATE 16

ACCESSION NUMBER: 1998-09561 BIOTECHDS

TITLE: New DNA encoding *Staphylococcus aureus* histidine-kinase;

used to screen compounds for antibiotic activity and as vaccines and to treat *Staphylococcus* infection in e.g. wounds and prostheses

AUTHOR: Wallis N G; Shilling L K; Warren R L

PATENT ASSIGNEE: SK-Beecham

LOCATION: Philadelphia, PA, USA; Brentford, Middlesex, UK.

PATENT INFO: EP 857787 12 Aug 1998

APPLICATION INFO: EP 1998-300829 4 Feb 1998

PRIORITY INFO: US 1997-37856 7 Feb 1997

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 1998-416009 [36]

AB An isolated DNA sequence (I) is claimed having at least 70% identity to a sequence encoding a 139 amino acid protein (II) (also claimed). Also claimed are: an isolated DNA sequence with at least 70% identity to a sequence encoding the same protein expressed by the histidine-kinase gene in *Staphylococcus aureus* WCUH29; a sequence encoding a protein whose sequence is at least 70% identical to (II); a DNA sequence complementary to (I); a vector comprising (I) and a host cell comprising this; a protein at least 70% identical to (II); antibody against (II); and an antagonist inhibiting the activity/expression of (II). (II) is used to treat an individual requiring histidine-kinase. The

antagonist can be used to inhibit it. (II) can also be used to diagnose disease related to expression or activity of (II) and as vaccines for and to treat *Staphylococcus aureus* infections. (I) and (II) are used to screen for compounds with antibiotic activity. They are also used in surgery and to treat wounds, and are also possible prophylactic antibiotics to prevent late deep infection after insertion of a prosthesis. (23pp)

L8 ANSWER 51 OF 58 MEDLINE on STN DUPLICATE 17  
ACCESSION NUMBER: 1998294055 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9632266  
TITLE: Transmembrane topology and histidine protein kinase activity of AgrC, the agr signal receptor in *Staphylococcus aureus*.  
AUTHOR: Lina G; Jarraud S; Ji G; Greenland T; Pedraza A; Etienne J; Novick R P; Vandenesch F  
CORPORATE SOURCE: UPRES EA1655, Faculte de Medecine Laennec, Lyon, France.. geralina@univ-lyon1.fr  
SOURCE: Molecular microbiology, (1998 May) 28 (3) 655-62.  
JOURNAL code: 8712028. ISSN: 0950-382X.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199809  
ENTRY DATE: Entered STN: 19981006  
Last Updated on STN: 19981006  
Entered Medline: 19980924

AB The agr P2 operon in *Staphylococcus aureus* codes for the elements of a density-sensing cassette made up of a typical two-component signalling system and its corresponding inducer. It is postulated that the autoinducer, a post-translationally modified octapeptide generated from the AgrD peptide, interacts with a receptor protein, coded by agrC, to transmit a signal via AgrA regulating expression of staphylococcal virulence genes through expression of agr RNA III. We show by analysis of PhoA fusions that AgrC is a transmembrane protein, and confirm using Western blotting that a 46 kDa protein corresponding to AgrC is present in the bacterial membrane. This protein is autophosphorylated on a histidine residue only in response to supernatants from an agr+ strain, and can also respond to the purified native octapeptide. A recombinant fusion protein where most of the N-terminal region of AgrC is replaced by the Escherichia coli maltose-binding protein is also autophosphorylated in response to stimulation by agr+ supernatants or purified octapeptide. We conclude that AgrC is the sensor molecule of a typical two-component signal system in *S. aureus*, and that the ligand-binding site of AgrC is probably located in the third extracellular loop of the protein.

L8 ANSWER 52 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN  
ACCESSION NUMBER: 1998:927981 SCISEARCH  
THE GENUINE ARTICLE: 143UN  
TITLE: Evidence for common sites of contact between the antisigma factor SpoIIAB and its partners SpoIIAA and the developmental transcription factor sigma(F) in *Bacillus subtilis*  
AUTHOR: Garsin D A; Paskowitz D M; Duncan L; Losick R (Reprint)  
CORPORATE SOURCE: HARVARD UNIV, BIOL LABS, DEPT MOL & CELLULAR BIOL, 16 DIVERS AVE, CAMBRIDGE, MA 02138 (Reprint); HARVARD UNIV, BIOL LABS, DEPT MOL & CELLULAR BIOL, CAMBRIDGE, MA 02138  
COUNTRY OF AUTHOR: USA  
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (4 DEC 1998) Vol. 284, No. 3, pp. 557-568.  
Publisher: ACADEMIC PRESS LTD, 24-28 OVAL RD, LONDON NW1

7DX, ENGLAND.  
ISSN: 0022-2836.  
DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE  
LANGUAGE: English  
REFERENCE COUNT: 50

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB The activity of the developmental transcription factor sigma(F) in *Bacillus subtilis* is governed by a switch involving the dual function protein SpoIIAB. SpoIIAB is an antisigma factor that forms complexes with sigma(F) and with an alternative partner protein SpoIIAA. SpoIIAB is also a protein kinase that can inactivate SpoIIAA by phosphorylating it on a serine residue. We sought to identify amino acids in SpoIIAB that are involved in the formation of the SpoIIAB-SpoIIAA complex by screening for mutants that were defective in the activation of sigma(F). This genetic screen, in combination with biochemical analysis and the construction of loss-of-sidechain (alanine substitution) mutants, led to the identification of amino acid side-chains in the N-terminal region of SpoIIAB that could contact SpoIIAA. Unexpectedly, the same amino acid side-chains (R20 and N50) that appear to touch SpoIIAA are required for binding to, and map represent sites of contact with, sigma(F). We propose that the N-terminal region of SpoIIAB forms a binding surface that is responsible for the formation of both the SpoIIAB-SpoIIAA and the SpoIIAB-sigma(F) complexes, and that in some cases the same amino acid side-chains contact both partner proteins. N50 is also the defining residue of a region of amino acid sequence homology known as the N-box that is shared by SpoIIAB and related serine protein kinases, as well as by members of a mechanistically dissimilar family of protein kinases that undergo autophosphorylation at a histidine residue. We discuss the implications of this finding for the mechanism of histidine autophosphorylation. (C) 1998 Academic Press.

L8 ANSWER 53 OF 58 MEDLINE on STN DUPLICATE 18  
ACCESSION NUMBER: 1998294999 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9631538  
TITLE: Cloning and characterization of an accessory gene regulator (agr)-like locus from *Staphylococcus epidermidis*.  
AUTHOR: Van Wamel W J; van Rossum G; Verhoef J;  
Vandenbroucke-Grauls C M; Fluit A C  
CORPORATE SOURCE: Eijkman-Winkler Institute for Microbiology, Infectious Diseases and Inflammation, Utrecht University, Netherlands.. w.j.b.vanwamel@lab.azu.nl  
SOURCE: FEMS microbiology letters, (1998 Jun 1) 163 (1) 1-9.  
Journal code: 7705721. ISSN: 0378-1097.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-Z49220  
ENTRY MONTH: 199807  
ENTRY DATE: Entered STN: 19980716  
Last Updated on STN: 19980716  
Entered Medline: 19980709

AB The presence of sequences related to the agr of *Staphylococcus aureus* was demonstrated in *Staphylococcus epidermidis* by agr-specific PCR, and Southern blot. The agr-like locus of *S. epidermidis* A086 was cloned and sequenced. An overall homology of 68% was found between the agr locus from *S. epidermidis* and *S. aureus*. The agr locus from *S. epidermidis* was organized similar to those from *S. aureus* and *S. lugdunensis*. The putative RNAII molecule contains four open reading frames, agr A, B, C and D. AgrA was a response regulator. AgrB showed homology with transducer and translocase molecules. AgrC is expected to act as a histidine protein kinase in which a leucine zipper is present. AgrD is presumably processed into an autoinducer peptide. The

putative RNAlII molecule contained an open reading frame encoding a putative 26 amino acid (aa) polypeptide, which differed in 3 aa from the RNAlII encoded delta-toxin of *S. aureus*. Kinetic studies showed that the production of this RNAlII was elevated during the post-exponential phase. delta-Toxin activity was demonstrated for 21 of 23 tested *S. epidermidis* strains. Kinetic studies of the production of delta-toxin showed that the toxin was produced during the post-exponential phase. Sequencing of *S. epidermidis* A097, which showed a delayed agr-response, revealed a truncated AgrC lacking the **histidine kinase** domain. These data indicate that an agr-like locus is active in *S. epidermidis* during the post-exponential phase.

L8 ANSWER 54 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN  
ACCESSION NUMBER: 1998:14702 SCISEARCH  
THE GENUINE ARTICLE: YL836  
TITLE: KapB is a lipoprotein required for KinB signal transduction and activation of the phosphorelay to sporulation in *Bacillus subtilis*  
AUTHOR: Dartois V; Djavakhishvili T; Hoch J A (Reprint)  
CORPORATE SOURCE: SCRIPPS CLIN & RES INST, DEPT MOL & EXPT MED, DIV CELLULAR BIOL, 10550 N TORREY PINES RD, LA JOLLA, CA 92037 (Reprint); SCRIPPS CLIN & RES INST, DEPT MOL & EXPT MED, DIV CELLULAR BIOL, LA JOLLA, CA 92037  
COUNTRY OF AUTHOR: USA  
SOURCE: MOLECULAR MICROBIOLOGY, (DEC 1997) Vol. 26, No. 5, pp. 1097-1108.  
Publisher: BLACKWELL SCIENCE LTD, OSNEY MEAD, OXFORD, OXON, ENGLAND OX2 0EL.  
ISSN: 0950-382X.  
DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE  
LANGUAGE: English  
REFERENCE COUNT: 39

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB KinB is one of the two major **histidine kinases** that provide phosphate input in the phosphorelay to produce SpoOA similar to P, the key transcription factor controlling the initiation of sporulation. A search for insertion mutants affected in activation of KinB-dependent sporulation led to the identification of the Igt locus encoding the lipoprotein glyceryltransferase required for the lipid modification of prolipoproteins before their cleavage and translocation across the cytoplasmic membrane. In parallel, a putative lipoprotein signal peptide cleavage site was detected in KapB, known to be strictly required for KinB-mediated sporulation and located downstream of KinB in a single transcription unit. Using PhoA peptide fusions, we have shown that KapB signal-peptide can direct active alkaline phosphatase to the outer surface of the cytoplasmic membrane in an LGT-dependent manner, strongly suggesting that KapB is a lipoprotein tethered to the outer face of the cytoplasmic membrane via a lipid anchor. As KapB proved to be dispensable for **expression** of the kinBkapB operon, a chimeric kinase was built consisting of KinA sensor domain fused to KinB kinase domain (KinA'-'B) to assess (i) the involvement of KapB in catalysis of the kinase reaction, and (ii) the ability of KinB to phosphorylate SpoOF in vitro. It was shown that KapB is dispensable for both *in vivo* and *in vitro* activation of the phosphorelay by the KinA'-'B chimera and that KinA'-'B phosphorylates SpoOF directly *in vitro*. Models for the role of KapB in regulating KinB activity are discussed.

L8 ANSWER 55 OF 58 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN  
ACCESSION NUMBER: 95:267936 SCISEARCH  
THE GENUINE ARTICLE: QR556  
TITLE: THE GENES INVOLVED IN PRODUCTION OF AND IMMUNITY TO

AUTHOR: SAKACIN-A, A BACTERIOCIN FROM LACTOBACILLUS-SAKE LB706  
CORPORATE SOURCE: AXELSSON L (Reprint); HOLCK A  
NORWEGIAN FOOD RES INST, MATFORSK, OSLOVEIEN 1, N-1430 AS,  
NORWAY (Reprint)  
COUNTRY OF AUTHOR: NORWAY  
SOURCE: JOURNAL OF BACTERIOLOGY, (APR 1995) Vol. 177, No. 8, pp.  
2125-2137.  
ISSN: 0021-9193.  
DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE  
LANGUAGE: ENGLISH  
REFERENCE COUNT: 56

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

AB Sakacin A is a small, heat-stable, antilisterial bacteriocin produced by *Lactobacillus sake* Lb706. The nucleotide sequence of a 8,668-bp fragment, shown to contain all information necessary for sakacin A production and immunity, was determined. The sequence revealed the presence of two divergently transcribed operons. The first encompassed the structural gene *sapA* (previously designated *sakA*) and *saiA*, which encoded a putative peptide of 90 amino acid residues. The second encompassed *sapK* (previously designated *sakB*), *sapR*, *sapT*, and *sapE*, *sapK* and *sapR* presumably encoded a **histidine kinase** and a response regulator with marked similarities to the *AgrB/AgrA* type of two-component signal-transducing systems. The putative *SapT* and *SapE* proteins shared similarity with the *Escherichia coli* hemolysin A-like signal, sequence-independent transport systems. *SapT* was the *HlyB* analog with homology to bacterial ATP-binding cassette exporters implicated in bacteriocin transport. Frameshift mutations and deletion analyses showed that *sapK* and *sapR* were necessary for both production and immunity, whereas *sapT* and *sapE* were necessary for production but not for immunity. The putative *SaiA* peptide was shown to be involved in the immunity to sakacin A. The region between the operons contained *IS1163*, a recently described *L. sake* insertion element. *IS1163* did not appear to be involved in **expression** of the *sap* genes. Northern (RNA) blot analysis revealed that the putative *SapK/SapR* system probably acts as a transcriptional activator on both operons. A 35-bp sequence, present upstream of the putative *sapA* promoter, and a similar sequence (30 of 35 nucleotides identical) upstream of *sapK* were shown to be necessary for proper **expression** and could thus be possible targets for transcriptional activation.

L8 ANSWER 56 OF 58 MEDLINE on STN  
ACCESSION NUMBER: 94161498 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8117074  
TITLE: The gene encoding plantaricin A, a bacteriocin from *Lactobacillus plantarum* C11, is located on the same transcription unit as an agr-like regulatory system.  
AUTHOR: Diep D B; Havarstein L S; Nissen-Meyer J; Nes I F  
CORPORATE SOURCE: Laboratory of Microbial Gene Technology, Agricultural University of Norway, As.  
SOURCE: Applied and environmental microbiology, (1994 Jan) 60 (1) 160-6.  
Journal code: 7605801. ISSN: 0099-2240.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-X75323  
ENTRY MONTH: 199403  
ENTRY DATE: Entered STN: 19940406  
Last Updated on STN: 19950206  
Entered Medline: 19940328  
AB Purification and amino acid sequencing of plantaricin A, a bacteriocin from *Lactobacillus plantarum* C11, revealed that maximum bacteriocin

activity is associated with the complementary action of two almost-identical peptides, alpha and beta (J. Nissen-Meyer, A. G. Larsen, K. Sletten, M. Daeschel, and I. F. Nes, J. Gen. Microbiol. 139:1973-1978, 1993). A 5-kb chromosomal HindIII restriction fragment containing the structural gene of plantaricin A was cloned and sequenced. Only one gene encoding plantaricin A was found. The gene, termed plnA, encodes a 48-amino-acid precursor peptide, of which the 22 and 23 C-terminal amino acids correspond to the purified peptides. Northern (RNA) blot analysis demonstrated that a probe complementary to the coding strand of the plantaricin A gene hybridized to a 3.3-kb mRNA transcript. Further analysis of the 3.3-kb transcript demonstrated that it contains three additional open reading frames (plnB, plnC and plnD) downstream of plnA. The DNA sequences of plnB, plnC, and plnD revealed that their products closely resemble members of bacterial two-component signal transduction systems. The strongest homology was found to the accessory gene regulatory (agr) system, which controls expression of exoproteins during post-exponential growth in *Staphylococcus aureus*. The finding that plnABCD are transcribed from a common promoter suggests that the biological role played by the bacteriocin is somehow related to the regulatory function of the two-component system located on the same operon.

L8 ANSWER 57 OF 58 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 1994:191537 BIOSIS  
DOCUMENT NUMBER: PREV199497204537  
TITLE: Identification of a two-component regulatory system in *Staphylococcus aureus* that controls the expression of surface components.  
AUTHOR(S): Bayles, Kenneth W.  
CORPORATE SOURCE: UMBC, Baltimore, MD 21228, USA  
SOURCE: Journal of Cellular Biochemistry Supplement, (1994) Vol. 0, No. 18 PART A, pp. 44.  
Meeting Info.: Keystone Symposium on Molecular Events in Microbial Pathogenesis. Santa Fe, New Mexico, USA. January 8-14, 1994.  
ISSN: 0733-1959.  
DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 2 May 1994  
Last Updated on STN: 3 May 1994

L8 ANSWER 58 OF 58 MEDLINE on STN

ACCESSION NUMBER: 94028916 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8215360  
TITLE: Cloning and nucleotide sequence of a gene from *Lactobacillus sake* Lb706 necessary for sakacin A production and immunity.  
AUTHOR: Axelsson L; Holck A; Birkeland S E; Aukrust T; Blom H  
CORPORATE SOURCE: MATFORSK, Norwegian Food Research Institute, As.  
SOURCE: Applied and environmental microbiology, (1993 Sep) 59 (9) 2868-75.  
Journal code: 7605801. ISSN: 0099-2240.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-X62978; GENBANK-X62979; GENBANK-X62980;  
GENBANK-X62981; GENBANK-X62986; GENBANK-X62987;  
GENBANK-X62988; GENBANK-X62989; GENBANK-X62990;  
GENBANK-Z21855  
ENTRY MONTH: 199311

ENTRY DATE: Entered STN: 19940117  
Last Updated on STN: 19950206  
Entered Medline: 19931110

AB Sakacin A is an antilisterial bacteriocin produced by *Lactobacillus sake* Lb706. In order to identify genes involved in sakacin A production and immunity, the plasmid fraction of *L. sake* Lb706 was shotgun cloned directly into a sakacin A-nonproducing and -sensitive variant, *L. sake* Lb706-B, by using the broad-host-range vector pVS2.. Two clones that produced sakacin A and were immune to the bacteriocin were obtained. A DNA fragment of approximately 1.8 kb, derived from a 60-kb plasmid of strain Lb706 and present in the inserts of both clones, was necessary for restoration of sakacin A production and immunity in strain Lb706-B. The sequence of the 1.8-kb fragment from one of the clones was determined. It contained one large open reading frame, designated sakB, potentially encoding a protein of 430 amino acid residues. Hybridization and nucleotide sequence analyses revealed that the cloned sakB complemented a mutated copy of sakB present in strain Lb706-B. The sakB gene mapped 1.6 kb from the previously cloned structural gene for sakacin A (sakA) on the 60-kb plasmid. The putative SakB protein shared 22% amino acid sequence identity (51% similarity if conservative changes are considered) to AgrB, the deduced amino acid sequence of the *Staphylococcus aureus* gene agrB. The polycistronic agr (accessory gene regulator) locus is involved in the regulation of exoprotein synthesis in *S. aureus*. Similar to the AgrB protein, SakB had some features in common with a family of transmembrane histidine protein kinases, involved in various adaptive response systems of bacteria. (ABSTRACT TRUNCATED AT 250 WORDS)

=> e wallis n g/au

E1	4	WALLIS N A/AU
E2	22	WALLIS N E/AU
E3	119	--> WALLIS N G/AU
E4	5	WALLIS N J/AU
E5	2	WALLIS N J H/AU
E6	1	WALLIS N R/AU
E7	15	WALLIS N T/AU
E8	2	WALLIS N Z/AU
E9	2	WALLIS NEIL R/AU
E10	1	WALLIS NG/AU
E11	16	WALLIS NICOLA/AU
E12	66	WALLIS NICOLA G/AU

=> s e3

L9 119 "WALLIS N G"/AU

=> e shilling l k/au

E1	1	SHILLING L A/AU
E2	1	SHILLING L J/AU
E3	28	--> SHILLING L K/AU
E4	8	SHILLING L M/AU
E5	1	SHILLING LILLESS MCPHERSON/AU
E6	4	SHILLING LISA/AU
E7	21	SHILLING LISA K/AU
E8	30	SHILLING LISA KATHLEEN/AU
E9	1	SHILLING LISA KETHLEEN/AU
E10	1	SHILLING LYNNDON/AU
E11	13	SHILLING M/AU
E12	1	SHILLING M A/AU

=> s e3-e9

L10 93 ("SHILLING L K"/AU OR "SHILLING L M"/AU OR "SHILLING LILLESS MCPHERSON"/AU OR "SHILLING LISA"/AU OR "SHILLING LISA K"/AU OR "SHILLING LISA KATHLEEN"/AU OR "SHILLING LISA KETHLEEN"/AU)

=> e mooney j l/au

E1	16	MOONEY J K/AU
E2	5	MOONEY J K JR/AU
E3	63	--> MOONEY J L/AU
E4	39	MOONEY J M/AU
E5	1	MOONEY J MATTHEW/AU
E6	17	MOONEY J P/AU
E7	48	MOONEY J R/AU
E8	5	MOONEY J ROBERT/AU
E9	49	MOONEY J S/AU
E10	30	MOONEY J W/AU
E11	4	MOONEY JAMES/AU
E12	1	MOONEY JAMES A/AU

=> s e3

L11	63	"MOONEY J L"/AU
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=> e debouck c/au

E1	1	DEBOUCHET J/AU
E2	6	DEBOUCHONY E T/AU
E3	416	--> DEBOUCK C/AU
E4	30	DEBOUCK C M/AU
E5	1	DEBOUCK C M */AU
E6	135	DEBOUCK CHRISTINE/AU
E7	19	DEBOUCK CHRISTINE M/AU
E8	11	DEBOUCK CHRISTINE MARIE/AU
E9	4	DEBOUCK D/AU
E10	47	DEBOUCK D G/AU
E11	12	DEBOUCK DANIEL G/AU
E12	2	DEBOUCK FERDINAND/AU

=> s e3

L12	416	"DEBOUCK C"/AU
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=> s e3-e8

L13	612	("DEBOUCK C"/AU OR "DEBOUCK C M"/AU OR "DEBOUCK C M */AU OR "DEBOUCK CHRISTINE"/AU OR "DEBOUCK CHRISTINE M"/AU OR "DEBOUCK CHRISTINE MARIE"/AU)
-----	-----	---

=> e zhong y y/au

E1	44	ZHONG Y W/AU
E2	53	ZHONG Y X/AU
E3	40	--> ZHONG Y Y/AU
E4	25	ZHONG Y Z/AU
E5	4	ZHONG YA/AU
E6	1	ZHONG YA LAN/AU
E7	8	ZHONG YA LING/AU
E8	6	ZHONG YA ZHEN/AU
E9	1	ZHONG YAFENG/AU
E10	2	ZHONG YA JUN/AU
E11	7	ZHONG YALAN/AU
E12	1	ZHONG YALI/AU

=> s e3

L14	40	"ZHONG Y Y"/AU
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=> e jaworski d d/au

E1	3	JAWORSKI D A/AU
E2	75	JAWORSKI D C/AU
E3	87	--> JAWORSKI D D/AU
E4	59	JAWORSKI D M/AU
E5	1	JAWORSKI DALPHNE/AU
E6	1	JAWORSKI DD/AU

E7 9 JAWORSKI DEBORAH/AU  
E8 21 JAWORSKI DEBORAH C/AU  
E9 64 JAWORSKI DEBORAH D/AU  
E10 34 JAWORSKI DEBORAH DEE/AU  
E11 21 JAWORSKI DIANE M/AU  
E12 2 JAWORSKI DON/AU

=> s e3-e10  
L15 276 ("JAWORSKI D D"/AU OR "JAWORSKI D M"/AU OR "JAWORSKI DALPHNE"/AU  
OR "JAWORSKI DD"/AU OR "JAWORSKI DEBORAH"/AU OR "JAWORSKI DEBORAH C"/AU  
OR "JAWORSKI DEBORAH D"/AU OR "JAWORSKI DEBORAH DEE"/AU  
)

=> e wang m/au  
E1 1 WANG LYNN HUANG/AU  
E2 1 WANG LYUAN/AU  
E3 6684 --> WANG M/AU  
E4 29 WANG M A/AU  
E5 279 WANG M B/AU  
E6 1168 WANG M C/AU  
E7 2 WANG M C C/AU  
E8 5 WANG M C H/AU  
E9 1 WANG M C M/AU  
E10 1 WANG M C T/AU  
E11 2 WANG M C W/AU  
E12 303 WANG M D/AU

=> s e3  
L16 6684 "WANG M"/AU

=> e throup j p/au  
E1 13 THROUP J/AU  
E2 1 THROUP J A/AU  
E3 55 --> THROUP J P/AU  
E4 19 THROUP JOHN/AU  
E5 1 THROUP JOHN A/AU  
E6 35 THROUP JOHN P/AU  
E7 5 THROUP JOHN PETER/AU  
E8 4 THROUPE P/AU  
E9 3 THROUVALAS A/AU  
E10 73 THROUVALAS N/AU  
E11 4 THROUVALAS N A/AU  
E12 14 THROUVALAS NICOLAS/AU

=> s e3-e7  
L17 115 ("THROUP J P"/AU OR "THROUP JOHN"/AU OR "THROUP JOHN A"/AU OR  
"THROUP JOHN P"/AU OR "THROUP JOHN PETER"/AU)

=> d his

(FILE 'HOME' ENTERED AT 11:59:47 ON 12 NOV 2004)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,  
LIFESCI' ENTERED AT 12:00:12 ON 12 NOV 2004

L1 1253188 S KINASE?  
L2 182160 S HISTIDINE  
L3 4732 S L1(A)L2  
L4 6785689 S CLON? OR EXPRESS? OR RECOMBINANT  
L5 249014 S STAPHYLOCOCCUS (A)AUREUS  
L6 163 S L3 AND L5  
L7 102 S L4 AND L6  
L8 58 DUP REM L7 (44 DUPLICATES REMOVED)  
E WALLIS N G/AU  
L9 119 S E3

L10                   E SHILLING L K/AU  
93 S E3-E9  
  E MOONEY J L/AU  
L11                   63 S E3  
  E DEBOUCK C/AU  
L12                   416 S E3  
L13                   612 S E3-E8  
  E ZHONG Y Y/AU  
L14                   40 S E3  
  E JAWORSKI D D/AU  
L15                   276 S E3-E10  
  E WANG M/AU  
L16                   6684 S E3  
  E THROUP J P/AU  
L17                   115 S E3-E7

=> s 18 or 19 or 110 or 111 or 113 or 114 or 115 or 116 or 117  
L18               7894 L8 OR L9 OR L10 OR L11 OR L13 OR L14 OR L15 OR L16 OR  
                 L17

=> s 16 and 118  
L19               72 L6 AND L18

=> dup rem 119  
PROCESSING COMPLETED FOR L19  
L20               59 DUP REM L19 (13 DUPLICATES REMOVED)

=> d 1-59 ibib

L20 ANSWER 1 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on  
STN  
ACCESSION NUMBER: 2004:517041 SCISEARCH  
THE GENUINE ARTICLE: 824CT  
TITLE: Identification of a novel two-component system in  
Streptococcus gordonii V288 involved in biofilm formation  
Zhang Y S; Lei Y; Khammanivong A; Herzberg M C (Reprint)  
AUTHOR: Univ Minnesota, Dept Oral Sci, 17-164 Moos Tower, 515  
CORPORATE SOURCE: Delaware St SE, Minneapolis, MN 55455 USA (Reprint); Univ  
Minnesota, Dept Oral Sci, Minneapolis, MN 55455 USA; Univ  
Minnesota, Mucosal & Vaccine Res Ctr, Minneapolis, MN  
55455 USA; Univ Minnesota, Sch Dent, Dept Oral Sci,  
Minneapolis, MN 55455 USA  
COUNTRY OF AUTHOR: USA  
SOURCE: INFECTION AND IMMUNITY, (JUN 2004) Vol. 72, No. 6, pp.  
3489-3494.  
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW,  
WASHINGTON, DC 20036-2904 USA.  
ISSN: 0019-9567.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 40  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L20 ANSWER 2 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on  
STN  
ACCESSION NUMBER: 2004:498290 SCISEARCH  
THE GENUINE ARTICLE: 822TE  
TITLE: Differential gene expression in response to  
hydrogen peroxide and the putative PerR regulon of  
Synechocystis sp strain PCC 6803  
AUTHOR: Li H; Singh A K; McIntyre L M; Sherman L A (Reprint)  
CORPORATE SOURCE: Purdue Univ, Dept Biol Sci, W Lafayette, IN 47907 USA  
(Reprint); Purdue Univ, Dept Agron, W Lafayette, IN 47907  
USA

COUNTRY OF AUTHOR: USA  
SOURCE: JOURNAL OF BACTERIOLOGY, (JUN 2004) Vol. 186, No. 11, pp. 3331-3345.  
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.  
ISSN: 0021-9193.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 75  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L20 ANSWER 3 OF 59 MEDLINE on STN  
ACCESSION NUMBER: 2004166238 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 15060046  
TITLE: Characterization of virulence factor regulation by SrrAB, a two-component system in *Staphylococcus aureus*.  
AUTHOR: Pragman Alexa A; Yarwood Jeremy M; Tripp Timothy J; Schlievert Patrick M  
CORPORATE SOURCE: Department of Microbiology, University of Minnesota Medical School, Minneapolis, Minnesota 55455, USA.  
CONTRACT NUMBER: T32 AI 07421 (NIAID)  
SOURCE: Journal of bacteriology, (2004 Apr) 186 (8) 2430-8.  
Journal code: 2985120R. ISSN: 0021-9193.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-AF260326  
ENTRY MONTH: 200405  
ENTRY DATE: Entered STN: 20040403  
Last Updated on STN: 20040525  
Entered Medline: 20040524

L20 ANSWER 4 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN  
ACCESSION NUMBER: 2004:271816 SCISEARCH  
THE GENUINE ARTICLE: 802HO  
TITLE: pbp2229-mediated nisin resistance mechanism in *Listeria monocytogenes* confers cross-protection to class IIa bacteriocins and affects virulence gene expression.  
AUTHOR: Gravesen A (Reprint); Kallipolitis B; Holmstrom K; Hoiby P E; Ramnath M; Knochel S  
CORPORATE SOURCE: Royal Vet & Agr Univ, LMC, Ctr Adv Food Studies, Dept Dairy & Food Sci, Rolighedsvej 30, DK-1958 Frederiksberg C, Denmark (Reprint); Royal Vet & Agr Univ, LMC, Ctr Adv Food Studies, Dept Dairy & Food Sci, DK-1958 Frederiksberg C, Denmark; Univ So Denmark, Dept Biochem & Mol Biol, DK-5230 Odense, Denmark; Bioneer A S, Dept Mol Characterizat, DK-2970 Horsholm, Denmark; Univ Stellenbosch, Dept Biochem, ZA-7602 Matieland, South Africa  
COUNTRY OF AUTHOR: Denmark; South Africa  
SOURCE: APPLIED AND ENVIRONMENTAL MICROBIOLOGY, (MAR 2004) Vol. 70, No. 3, pp. 1669-1679.  
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.  
ISSN: 0099-2240.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 50  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L20 ANSWER 5 OF 59 MEDLINE on STN

ACCESSION NUMBER: 2004212976 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 15109784  
TITLE: Regulation of virulence determinants in *Staphylococcus aureus*: complexity and applications.  
AUTHOR: Bronner Stephane; Monteil Henri; Prevost Gilles  
CORPORATE SOURCE: Institut de Bacteriologie, Faculte de Medecine, Universite Louis Pasteur - Hopitaux, Universitaires de Strasbourg, 3, rue Koeberle, F-67000 Strasbourg, France.  
SOURCE: FEMS microbiology reviews, (2004 May) 28 (2) 183-200. Ref: 114  
PUB. COUNTRY: Journal code: 8902526. ISSN: 0168-6445.  
Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, ACADEMIC)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200407  
ENTRY DATE: Entered STN: 20040428  
Last Updated on STN: 20040703  
Entered Medline: 20040702

L20 ANSWER 6 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN  
ACCESSION NUMBER: 2004:139965 SCISEARCH  
THE GENUINE ARTICLE: 769FL  
TITLE: Regulation of virulence determinants in vitro and in vivo in *Staphylococcus aureus*  
AUTHOR: Cheung A L (Reprint); Bayer A S; Zhang G Y; Gresham H; Xiong Y Q  
CORPORATE SOURCE: Dartmouth Coll Sch Med, Dept Microbiol, Hanover, NH 03755 USA (Reprint); Univ Calif Los Angeles, Harbor Med Ctr, Res & Educ Inst, Torrance, CA 90502 USA; Univ Calif Los Angeles, Sch Med, Los Angeles, CA 90024 USA; Natl Jewish Med & Res Ctr, Integrated Dept Immunol, Denver, CO 80206 USA; Univ New Mexico, Sch Med, Dept Microbiol & Mol Genet, Albuquerque, NM 87131 USA  
COUNTRY OF AUTHOR: USA  
SOURCE: FEMS IMMUNOLOGY AND MEDICAL MICROBIOLOGY, (15 JAN 2004)  
Vol. 40, No. 1, pp. 1-9.  
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.  
ISSN: 0928-8244.  
DOCUMENT TYPE: General Review; Journal  
LANGUAGE: English  
REFERENCE COUNT: 53  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L20 ANSWER 7 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2004-00275 BIOTECHDS  
TITLE: New isolated nucleic acid encoding a peptide that kills both wild type pneumococci and a strain of *Pneumococcus* that is autolysin deficient, useful for treating or preventing bacterial infections or inflammations;  
recombinant protein production for use in disease therapy and drug screening  
AUTHOR: NOVAK R; TUOMANEN E I  
PATENT ASSIGNEE: ST JUDE CHILDREN'S RES HOSPITAL  
PATENT INFO: US 6630583 7 Oct 2003  
APPLICATION INFO: US 2000-493940 28 Jan 2000  
PRIORITY INFO: US 2000-493940 28 Jan 2000; US 1998-84399 6 May 1998  
DOCUMENT TYPE: Patent  
LANGUAGE: English

OTHER SOURCE: WPI: 2003-810553 [76]

L20 ANSWER 8 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2003-18374 BIOTECHDS  
TITLE: New oligonucleotide probes which specifically hybridize to  
*Staphylococcus aureus histidine*  
kinase essential genes, useful for developing  
antibacterial agents, or as probes for detecting the presence  
a particular gene;  
drug screening for use in bacterium infection diagnosis  
and gene therapy  
AUTHOR: BENTON B; MALOUIN F; MARTIN P K; SCHMID M B; SUN D  
PATENT ASSIGNEE: ESSENTIAL THERAPEUTICS INC  
PATENT INFO: US 6514746 4 Feb 2003  
APPLICATION INFO: US 1998-82077 20 May 1998  
PRIORITY INFO: US 1998-82077 20 May 1998; US 1995-3798 15 Sep 1995  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2003-478763 [45]

L20 ANSWER 9 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on  
STN  
ACCESSION NUMBER: 2003:1087573 SCISEARCH  
THE GENUINE ARTICLE: 751GL  
TITLE: Chemical communication among bacteria  
AUTHOR: Taga M E; Bassler B L (Reprint)  
CORPORATE SOURCE: Princeton Univ, Dept Mol Biol, Princeton, NJ 08544 USA  
(Reprint)  
COUNTRY OF AUTHOR: USA  
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE  
UNITED STATES OF AMERICA, (25 NOV 2003) Vol. 100, Supp.  
[2], pp. 14549-14554.  
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW,  
WASHINGTON, DC 20418 USA.  
ISSN: 0027-8424.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 65  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L20 ANSWER 10 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN  
ACCESSION NUMBER: 2003:224073 SCISEARCH  
THE GENUINE ARTICLE: 652DR  
TITLE: Detection of secreted peptides by using hypothesis-driven  
multistage mass spectrometry  
AUTHOR: Kalkum M; Lyon G J; Chait B T (Reprint)  
CORPORATE SOURCE: Rockefeller Univ, Lab Mass Spectrometry & Gaseous Chem,  
1230 York Ave, New York, NY 10021 USA (Reprint);  
Rockefeller Univ, Lab Mass Spectrometry & Gaseous Chem,  
New York, NY 10021 USA; Rockefeller Univ, Selma & Lawrence  
Ruben Lab Synthet Prot Chem, New York, NY 10021 USA  
COUNTRY OF AUTHOR: USA  
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE  
UNITED STATES OF AMERICA, (4 MAR 2003) Vol. 100, No. 5,  
pp. 2795-2800.  
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW,  
WASHINGTON, DC 20418 USA.  
ISSN: 0027-8424.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 53  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L20 ANSWER 11 OF 59 MEDLINE on STN  
ACCESSION NUMBER: 2003570426 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 14651645  
TITLE: Constitutive expression of PcsB suppresses the requirement for the essential VicR (YycF) response regulator in *Streptococcus pneumoniae* R6.  
AUTHOR: Ng Wai-Leung; Robertson Gregory T; Kazmierczak Krystyna M; Zhao Jingyong; Gilmour Raymond; Winkler Malcolm E  
CORPORATE SOURCE: Department of Biology, Indiana University, Jordan Hall 142, Bloomington, IN 47405, USA.  
SOURCE: Molecular microbiology, (2003 Dec) 50 (5) 1647-63.  
JOURNAL code: 8712028. ISSN: 0950-382X.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200403  
ENTRY DATE: Entered STN: 20031216  
Last Updated on STN: 20040302  
Entered Medline: 20040301

L20 ANSWER 12 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2003:776164 HCAPLUS  
DOCUMENT NUMBER: 139:359758  
TITLE: Genes controlled by the essential YycG/YycF two-component system of *Bacillus subtilis* revealed through a novel hybrid regulator approach  
AUTHOR(S): Howell, Alistair; Dubrac, Sarah; Andersen, Kasper Krogh; Noone, David; Fert, Juliette; Msadek, Tarek; Devine, Kevin  
CORPORATE SOURCE: Department of Genetics, Smurfit Institute, Trinity College Dublin, Dublin, 2, Ire.  
SOURCE: Molecular Microbiology (2003), 49(6), 1639-1655  
CODEN: MOMIEE; ISSN: 0950-382X  
PUBLISHER: Blackwell Publishing Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 13 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN  
ACCESSION NUMBER: 2003:513309 SCISEARCH  
THE GENUINE ARTICLE: 687GZ  
TITLE: Autoinduction and signal transduction in the regulation of staphylococcal virulence  
AUTHOR: Novick R P (Reprint)  
CORPORATE SOURCE: NYU, Sch Med, Dept Microbiol, Skirball Inst, Program Mol Pathogenesis, New York, NY 10016 USA (Reprint); NYU, Sch Med, Dept Med, Skirball Inst, Program Mol Pathogenesis, New York, NY 10016 USA  
COUNTRY OF AUTHOR: USA  
SOURCE: MOLECULAR MICROBIOLOGY, (JUN 2003) Vol. 48, No. 6, pp. 1429-1449.  
Publisher: BLACKWELL PUBLISHING LTD, 9600 GARSINGTON RD, OXFORD OX4 2DG, OXON, ENGLAND.  
ISSN: 0950-382X.  
DOCUMENT TYPE: General Review; Journal  
LANGUAGE: English  
REFERENCE COUNT: 126  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L20 ANSWER 14 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2004-03939 BIOTECHDS

TITLE: Isolation and characterization of inhibitors of the essential histidine kinase, YycG in *Bacillus subtilis* and *Staphylococcus aureus*; vector-mediated gene transfer and expression in host cell for antibiotic screening and antibiotic-resistant bacterium infection therapy

AUTHOR: WATANABE T; HASHIMOTO Y; YAMAMOTO K; HIRAO K; ISHIHAMA A; HINO M; UTSUMI R

CORPORATE SOURCE: Kinki Univ; Nippon Inst Biol Sci; Fujisawa Pharmaceut Co Ltd

LOCATION: Utsumi R, Kinki Univ, Grad Sch Agr, Dept Biosci and Biotechnol, 3327-204 Nakamachi, Nara 6318505, Japan

SOURCE: JOURNAL OF ANTIBIOTICS; (2003) 56, 12, 1045-1052

ISSN: 0021-8820

DOCUMENT TYPE: Journal

LANGUAGE: English

L20 ANSWER 15 OF 59 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.  
on STN

ACCESSION NUMBER: 2003448363 EMBASE

TITLE: Turning virulence on and off in *Staphylococci*.

AUTHOR: Muir T.W.

CORPORATE SOURCE: Dr. T.W. Muir, Lab. of Synthetic Protein Chemistry, The Rockefeller University, 1230 York Avenue, New York, NY 10021, United States. muirt@rockefeller.edu

SOURCE: Journal of Peptide Science, (2003) 9/10 (612-619).  
Refs: 21  
ISSN: 1075-2617 CODEN: JPSIEI

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 004 Microbiology  
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

L20 ANSWER 16 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:965696 HCAPLUS

DOCUMENT NUMBER: 139:194031

TITLE: Pathogenicity and histidine kinases : approaches toward the development of a new generation of antibiotics

AUTHOR(S): Hubbard, J.; Burnham, M. K. R.; Throup, J. P.

CORPORATE SOURCE: Computational and Structural Sciences, GlaxoSmithKline, Harlow, UK

SOURCE: Histidine Kinases in Signal Transduction (2003), 459-481. Editor(s): Inouye, Masayori; Dutta, Rinku. Elsevier Science: San Diego, Calif.

CODEN: 69DIUS; ISBN: 0-12-372484-8

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 17 OF 59 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2003373501 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12867749

TITLE: Biochemical characterization of the first essential two-component signal transduction system from *Staphylococcus aureus* and *Streptococcus pneumoniae*.

AUTHOR: Clausen Valerie A; Bae Weonhye; Throup John; Burnham Martin K R; Rosenberg Martin; Wallis Nicola G

CORPORATE SOURCE: Antimicrobials and Host Defense, GlaxoSmithKline Pharmaceuticals, Collegeville, PA, USA.

SOURCE: Journal of molecular microbiology and biotechnology, (2003)

5 (4) 252-60.  
Journal code: 100892561. ISSN: 1464-1801.  
PUB. COUNTRY: Switzerland  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200309  
ENTRY DATE: Entered STN: 20030812  
Last Updated on STN: 20030905  
Entered Medline: 20030904

L20 ANSWER 18 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on  
STN  
ACCESSION NUMBER: 2003:517200 BIOSIS  
DOCUMENT NUMBER: PREV200300519820  
TITLE: Subcellular localization of SrrAB, a novel two-component  
regulatory system in *Staphylococcus*  
*aureus*.  
AUTHOR(S): Pragman, A. A. [Reprint Author]; Schlievert, P. M. [Reprint  
Author]  
CORPORATE SOURCE: University of Minnesota, Minneapolis, MN, USA  
SOURCE: Abstracts of the General Meeting of the American Society  
for Microbiology, (2003) Vol. 103, pp. B-066.  
<http://www.asmusa.org/mtgsrc/generalmeeting.htm>. cd-rom.  
Meeting Info.: 103rd American Society for Microbiology  
General Meeting. Washington, DC, USA. May 18-22, 2003.  
American Society for Microbiology.  
ISSN: 1060-2011 (ISSN print).  
DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 5 Nov 2003  
Last Updated on STN: 5 Nov 2003

L20 ANSWER 19 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on  
STN  
ACCESSION NUMBER: 2003:517239 BIOSIS  
DOCUMENT NUMBER: PREV200300519832  
TITLE: Two-component gene regulation in the biology of  
*Enterococcus faecalis*.  
AUTHOR(S): Hancock, L. E. [Reprint Author]; Perego, M. [Reprint  
Author]  
CORPORATE SOURCE: Scripps Research Institute, La Jolla, CA, USA  
SOURCE: Abstracts of the General Meeting of the American Society  
for Microbiology, (2003) Vol. 103, pp. B-078.  
<http://www.asmusa.org/mtgsrc/generalmeeting.htm>. cd-rom.  
Meeting Info.: 103rd American Society for Microbiology  
General Meeting. Washington, DC, USA. May 18-22, 2003.  
American Society for Microbiology.  
ISSN: 1060-2011 (ISSN print).  
DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 5 Nov 2003  
Last Updated on STN: 5 Nov 2003

L20 ANSWER 20 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2002-10378 BIOTECHDS  
TITLE: Assay for detecting compounds that modulates  
*histidine kinase* activity, by contacting  
compound with kinase and substrate, and monitoring the rate  
or absolute amount of phosphate transfer by kinase to the  
substrate;  
plasmid pMal- (RTM) -c2-mediated gene transfer and

expression in *Escherichia coli* for drug screening

AUTHOR: GOLDSCHMIDT R; LOELOFF M  
PATENT ASSIGNEE: GOLDSCHMIDT R; LOELOFF M  
PATENT INFO: US 2002004214 10 Jan 2002  
APPLICATION INFO: US 1999-733731 21 Dec 1999  
PRIORITY INFO: US 2000-733731 8 Dec 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-171025 [22]

L20 ANSWER 21 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN

ACCESSION NUMBER: 2002:359080 SCISEARCH  
THE GENUINE ARTICLE: 543NH  
TITLE: rgf encodes a novel two-component signal transduction  
system of *Streptococcus agalactiae*  
AUTHOR: Spellerberg B (Reprint); Rozdzinski E; Martin S;  
Weber-Heynemann J; Lutticken R  
CORPORATE SOURCE: Univ Ulm, Dept Med Microbiol & Hyg, Robert Koch Str 8,  
D-89081 Ulm, Germany (Reprint); Univ Ulm, Dept Med  
Microbiol & Hyg, D-89081 Ulm, Germany; Univ Hosp Aachen,  
Inst Med Microbiol, D-52057 Aachen, Germany; Univ Hosp  
Aachen, Natl Reference Ctr Streptococci, D-52057 Aachen,  
Germany  
COUNTRY OF AUTHOR: Germany  
SOURCE: INFECTION AND IMMUNITY, (MAY 2002) Vol. 70, No. 5, pp.  
2434-2440.  
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW,  
WASHINGTON, DC 20036-2904 USA.  
ISSN: 0019-9567.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 32  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L20 ANSWER 22 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN

ACCESSION NUMBER: 2002:652704 SCISEARCH  
THE GENUINE ARTICLE: 579BC  
TITLE: Recent progress in *Bacillus subtilis* two-component  
regulation  
AUTHOR: Ogura M; Tanaka T (Reprint)  
CORPORATE SOURCE: Tokai Univ, Sch Marine Sci & Technol, Dept Marine Sci,  
Orido 3-20-1, Shizuoka 4248610, Japan (Reprint); Tokai  
Univ, Sch Marine Sci & Technol, Dept Marine Sci, Shizuoka  
4248610, Japan  
COUNTRY OF AUTHOR: Japan  
SOURCE: FRONTIERS IN BIOSCIENCE, (AUG 2002) Vol. 7, pp.  
D1815-D1824.  
Publisher: FRONTIERS IN BIOSCIENCE INC, C/O NORTH SHORE  
UNIV HOSPITAL, BIOMEDICAL RESEARCH CENTER, 350 COMMUNITY  
DR, MANHASSET, NY 11030 USA.  
ISSN: 1093-9946.  
DOCUMENT TYPE: General Review; Journal  
LANGUAGE: English  
REFERENCE COUNT: 77  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L20 ANSWER 23 OF 59 MEDLINE on STN

ACCESSION NUMBER: 2002080831 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11807070  
TITLE: Repression of the *Staphylococcus aureus*  
accessory gene regulator in serum and in vivo.  
AUTHOR: Yarwood Jeremy M; McCormick John K; Paustian Michael L;

CORPORATE SOURCE: Kapur Vivek; Schlievert Patrick M  
Department of Microbiology, Medical School, University of Minnesota, Minneapolis, Minnesota, USA.  
CONTRACT NUMBER: HL36611 (NHLBI)  
SOURCE: Journal of bacteriology, (2002 Feb) 184 (4) 1095-101.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200203  
ENTRY DATE: Entered STN: 20020128  
Last Updated on STN: 20020320  
Entered Medline: 20020319

L20 ANSWER 24 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN  
ACCESSION NUMBER: 2002:267761 BIOSIS  
DOCUMENT NUMBER: PREV200200267761  
TITLE: Histidine kinases as targets for new antimicrobial agents.  
AUTHOR(S): Matsushita, Masayuki [Reprint author]; Janda, Kim D. [Reprint author]  
CORPORATE SOURCE: Department of Chemistry, Scripps Research Institute and Skaggs Institute for Chemical Biology, 10550 N. Torrey Pines Road, BCC-582, La Jolla, CA, 92037, USA  
kdjanda@scripps.edu  
SOURCE: Bioorganic and Medicinal Chemistry, (April, 2002) Vol. 10, No. 4, pp. 855-867. print.  
ISSN: 0968-0896.  
DOCUMENT TYPE: Article  
LANGUAGE: General Review; (Literature Review)  
ENTRY DATE: Entered STN: 1 May 2002  
Last Updated on STN: 1 May 2002

L20 ANSWER 25 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN  
ACCESSION NUMBER: 2002:756564 SCISEARCH  
THE GENUINE ARTICLE: 591TY  
TITLE: Two-component and phosphorelay signal-transduction systems as therapeutic targets  
AUTHOR: Stephenson K (Reprint); Hoch J A  
CORPORATE SOURCE: Scripps Clin & Res Inst, Dept Mol & Expt Med, MEM-116, 10550 N Torrey Pines Rd, La Jolla, CA 92037 USA (Reprint); Scripps Clin & Res Inst, Dept Mol & Expt Med, La Jolla, CA 92037 USA  
COUNTRY OF AUTHOR: USA  
SOURCE: CURRENT OPINION IN PHARMACOLOGY, (OCT 2002) Vol. 2, No. 5, pp. 507-512.  
Publisher: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND.  
ISSN: 1471-4892.  
DOCUMENT TYPE: General Review; Journal  
LANGUAGE: English  
REFERENCE COUNT: 63  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L20 ANSWER 26 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2002:858990 HCAPLUS  
DOCUMENT NUMBER: 138:148485  
TITLE: Regulatory relationship of two-component and ABC transport systems and clustering of their genes in the *Bacillus/Clostridium* group, suggest a functional link

AUTHOR(S): between them  
Joseph, Pascale; Fichant, Gwennaelle; Quentin, Yves;  
Denizot, Francois  
CORPORATE SOURCE: Laboratoire de Chimie Bacterienne, Institut de  
Biologie Structurale et Microbiologie, CNRS 31,  
Marseille, 13402, Fr.  
SOURCE: Journal of Molecular Microbiology and Biotechnology  
(2002), 4(5), 503-513  
CODEN: JMMBFF; ISSN: 1464-1801  
PUBLISHER: Horizon Scientific Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 27 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN  
ACCESSION NUMBER: 2002:602183 SCISEARCH  
THE GENUINE ARTICLE: 571KL  
TITLE: Virulence- and antibiotic resistance-associated  
two-component signal transduction systems of Gram-positive  
pathogenic bacteria as targets for antimicrobial therapy  
Stephenson K; Hoch J A (Reprint)  
CORPORATE SOURCE: Scripps Clin & Res Inst, Dept Mol & Expt Med, Div Cellular  
Biol, MEM-116, 10550 N Torrey Pines Rd, La Jolla, CA 92037  
USA (Reprint); Scripps Clin & Res Inst, Dept Mol & Expt  
Med, Div Cellular Biol, La Jolla, CA 92037 USA  
COUNTRY OF AUTHOR: USA  
SOURCE: PHARMACOLOGY & THERAPEUTICS, (FEB-MAR 2002) Vol. 93, No.  
2-3, pp. 293-305.  
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD,  
LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.  
ISSN: 0163-7258.  
DOCUMENT TYPE: Article; Journal  
LANGUAGE: English  
REFERENCE COUNT: 92  
\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L20 ANSWER 28 OF 59' HCAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2002:613874 HCAPLUS  
TITLE: Turning virulence on and off in Staphylococci  
AUTHOR(S): Muir, Tom W.  
CORPORATE SOURCE: Laboratory of Synthetic Protein Chemistry, Rockefeller  
University, New York City, NY, 10021, USA  
SOURCE: Abstracts of Papers, 224th ACS National Meeting,  
Boston, MA, United States, August 18-22, 2002 (2002),  
BIOL-102. American Chemical Society: Washington, D.  
C.  
CODEN: 69CZPZ  
DOCUMENT TYPE: Conference; Meeting Abstract  
LANGUAGE: English

L20 ANSWER 29 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on  
STN  
ACCESSION NUMBER: 2001:452628 BIOSIS  
DOCUMENT NUMBER: PREV200100452628  
TITLE: Histidine kinase of  
Staphylococcus aureus.  
AUTHOR(S): Wallis, Nicola Gail [Inventor]; Traini, Christopher Michael  
[Inventor]; Kosmatka, Anna Lisa [Inventor]; Shilling,  
Lisa Kathleen [Inventor]; Warren, Richard Lloyd  
[Inventor]  
CORPORATE SOURCE: ASSIGNEE: SmithKline Beecham Corporation, Philadelphia, PA,  
USA; SmithKline Beecham plc, Boreford, UK

PATENT INFORMATION: US 6270992 August 07, 2001  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (Aug. 7, 2001) Vol. 1249, No. 1. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 26 Sep 2001  
Last Updated on STN: 22 Feb 2002

L20 ANSWER 30 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on  
STN  
ACCESSION NUMBER: 2001:378355 BIOSIS  
DOCUMENT NUMBER: PREV200100378355  
TITLE: Histidine kinase, 636 HK, of  
staphylococcus aureus.  
AUTHOR(S): Burnham, Martin K R [Inventor]; Palmer, Leslie Marie  
[Inventor]; Throup, John Peter [Inventor, Reprint  
author]; Van Horn, Stephanie [Inventor]; Warren, Richard  
Lloyd [Inventor]  
CORPORATE SOURCE: Royersford, PA, USA  
ASSIGNEE: SmithKline Beecham Corporation  
PATENT INFORMATION: US 6194174 February 27, 2001  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (Feb. 27, 2001) Vol. 1243, No. 4. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 8 Aug 2001  
Last Updated on STN: 19 Feb 2002

L20 ANSWER 31 OF 59 MEDLINE on STN  
ACCESSION NUMBER: 2001469003 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11513618  
TITLE: The srhSR gene pair from *Staphylococcus*  
*aureus*: genomic and proteomic approaches to the  
identification and characterization of gene function.  
AUTHOR: Throup J P; Zappacosta F; Lunsford R D; Annan R  
S; Carr S A; Lonsdale J T; Bryant A P; McDevitt D;  
Rosenberg M; Burnham M K  
CORPORATE SOURCE: Anti-infectives Research, GlaxoSmithKline Pharmaceuticals  
Research and Development, Collegeville, Pennsylvania 19426,  
USA.. John\_Throup-1@sbphrd.com  
SOURCE: Biochemistry, (2001 Aug 28) 40 (34) 10392-401.  
Journal code: 0370623. ISSN: 0006-2960.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200109  
ENTRY DATE: Entered STN: 20010830  
Last Updated on STN: 20030325  
Entered Medline: 20010927

L20 ANSWER 32 OF 59 MEDLINE on STN  
ACCESSION NUMBER: 2001337274 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11136460  
TITLE: Group A streptococcal growth phase-associated virulence  
factor regulation by a novel operon (Fas) with homologies  
to two-component-type regulators requires a small RNA  
molecule.  
AUTHOR: Kreikemeyer B; Boyle M D; Buttaro B A; Heinemann M;  
Podbielski A  
CORPORATE SOURCE: Department of Medical Microbiology and Hygiene, University  
Hospital Ulm, Robert-Koch-Str. 8, D-89081 Ulm, Germany.

SOURCE: Molecular microbiology, (2001 Jan) 39 (2) 392-406.  
Journal code: 8712028. ISSN: 0950-382X.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200106  
ENTRY DATE: Entered STN: 20010618  
Last Updated on STN: 20010618  
Entered Medline: 20010614

L20 ANSWER 33 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2001:455510 HCAPLUS  
DOCUMENT NUMBER: 135:192773  
TITLE: Characterization of bacteriocin N15 produced by  
Enterococcus faecium N15 and cloning of the  
related genes  
AUTHOR(S): Losteinkit, Chanvadee; Uchiyama, Keiji; Ochi,  
Shuichiro; Takaoka, Tomoyo; Nagahisa, Keisuke; Shioya,  
Suteaki  
CORPORATE SOURCE: Department of Biotechnology, Graduate School of  
Engineering, Osaka University, Suita, 565-0871, Japan  
SOURCE: Journal of Bioscience and Bioengineering (2001),  
91(4), 390-395  
CODEN: JBBIF6; ISSN: 1389-1723  
PUBLISHER: Society for Bioscience and Bioengineering, Japan  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 34 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
DUPLICATE 2  
ACCESSION NUMBER: 2001-03236 BIOTECHDS  
TITLE: Histidine-kinase polypeptides and  
polynucleotides, useful for treating bacterial infections  
caused by *Staphylococcus aureus* such as  
otitis media, thyroiditis, empyema and for screening  
antibacterial compounds;  
the use of recombinant histidine-  
kinase  
AUTHOR: Throup J P; Palmer L M; Burnham M K; Warren R L;  
van Horn S  
PATENT ASSIGNEE: SK-Beecham  
LOCATION: Philadelphia, PA, USA; Brentford, UK.  
PATENT INFO: WO 2000068360 16 Nov 2000  
APPLICATION INFO: WO 2000-US12862 11 May 2000  
PRIORITY INFO: US 1999-310275 12 May 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2001-016089 [02]

L20 ANSWER 35 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on  
STN  
ACCESSION NUMBER: 2001:239703 BIOSIS  
DOCUMENT NUMBER: PREV200100239703  
TITLE: Sensor histidine kinase of  
*Staphylococcus Aureus*.  
AUTHOR(S): Wallis, Nicola Gail [Inventor]  
CORPORATE SOURCE: ASSIGNEE: SmithKline Beecham Corporation  
PATENT INFORMATION: US 6127147 October 03, 2000  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (Oct. 3, 2000) Vol. 1239, No. 1. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 16 May 2001  
Last Updated on STN: 18 Feb 2002

L20 ANSWER 36 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN  
ACCESSION NUMBER: 2001:70585 BIOSIS  
DOCUMENT NUMBER: PREV200100070585  
TITLE: Sensor histidine kinase of *Staphylococcus aureus*.  
AUTHOR(S): Wallis, Nicola Gail [Inventor]  
CORPORATE SOURCE: ASSIGNEE: SmithKline Beecham Corporation; SmithKline Beecham, p.l.c., UK  
PATENT INFORMATION: US 6071894 June 06, 2000  
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (June 6, 2000) Vol. 1235, No. 1. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 7 Feb 2001  
Last Updated on STN: 12 Feb 2002

L20 ANSWER 37 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2001-00945 BIOTECHDS  
TITLE: Histidine-kinase family polypeptides obtained from *Staphylococcus aureus*, useful for developing antibacterial compounds; vector-mediated gene transfer and expression in host cell, antibody, agonist and antagonist, appl. cancer and bacterium infection therapy  
AUTHOR: Wallis N G  
PATENT ASSIGNEE: SK-Beecham  
LOCATION: Philadelphia, PA, USA.  
PATENT INFO: WO 2000056865 28 Sep 2000  
APPLICATION INFO: WO 2000-US6206 9 Mar 2000  
PRIORITY INFO: US 1999-274058 22 Mar 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2000-638259 [61]

L20 ANSWER 38 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 2001-00532 BIOTECHDS  
TITLE: New histidine-kinase polypeptide and polynucleotide, useful for treating, preventing or diagnosing microbial diseases, especially infections caused by *Staphylococcus aureus*, e.g. otitis media, thyroiditis or wound infection; vector-mediated gene transfer and expression in host cell, antibody, agonist and antagonist  
AUTHOR: Wallis N G  
PATENT ASSIGNEE: SK-Beecham  
LOCATION: Philadelphia, PA, USA.  
PATENT INFO: WO 2000056154 28 Sep 2000  
APPLICATION INFO: WO 2000-US6133 8 Mar 2000  
PRIORITY INFO: US 1999-272414 19 Mar 1999  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2000-611569 [58]

L20 ANSWER 39 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2000:814336 HCAPLUS  
DOCUMENT NUMBER: 133:359212  
TITLE: *Staphylococcus aureus*

two-component signal transduction histidine  
 kinase-related 509HK proteins and  
 polynucleotides for screening of antibacterial agents  
 INVENTOR(S) : Bae, Weonhye; Van Horn, Stephanie; Warren, Richard L.;  
 Biswas, Sanjoy; Throup, John P.; Burnham,  
 Martin K. R.  
 PATENT ASSIGNEE(S) : SmithKline Beecham Corporation, USA; SmithKline  
 Beecham PLC  
 SOURCE: PCT Int. Appl., 37 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000067783	A1	20001116	WO 2000-US11917	20000503
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6406889	B1	20020618	US 2000-564954	20000504
PRIORITY APPLN. INFO.:			US 1999-132935P	P 19990506
REFERENCE COUNT:	2	THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

L20 ANSWER 40 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2000:814249 HCAPLUS  
 DOCUMENT NUMBER: 133:359809  
 TITLE: Cloning, sequencing and expression  
 of *Staphylococcus aureus*  
 histidine kinase 0623HK and its  
 therapeutic applications  
 INVENTOR(S) : Bae, Weonhye; Van Horn, Stephanie; Warren, Richard L.;  
 Biswas, Sanjoy; Throup, John P.; Burnham,  
 Martin K. R.  
 PATENT ASSIGNEE(S) : SmithKline Beecham Corporation, USA; SmithKline  
 Beecham PLC  
 SOURCE: PCT Int. Appl., 40 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000067575	A1	20001116	WO 2000-US12046	20000503
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			US 1999-132759P	P 19990506
REFERENCE COUNT:	1	THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

L20 ANSWER 41 OF 59 MEDLINE on STN  
 ACCESSION NUMBER: 2001284536 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 11087872  
 TITLE: Rational design of a global inhibitor of the virulence  
 response in *Staphylococcus aureus*,  
 based in part on localization of the site of inhibition to  
 the receptor-histidine kinase, AgrC.  
 AUTHOR: Lyon G J; Mayville P; Muir T W; Novick R P  
 CORPORATE SOURCE: Laboratory of Synthetic Protein Chemistry, The Rockefeller

University, 1230 York Avenue, New York, NY 10021, USA.

CONTRACT NUMBER: AI 42783 (NIAID)  
GM07739 (NIGMS)

SOURCE: Proceedings of the National Academy of Sciences of the  
United States of America, (2000 Nov 21) 97 (24) 13330-5.  
Journal code: 7505876. ISSN: 0027-8424.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200105  
ENTRY DATE: Entered STN: 20010529  
Last Updated on STN: 20010529  
Entered Medline: 20010524

L20 ANSWER 42 OF 59 MEDLINE on STN

ACCESSION NUMBER: 2000100755 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10633099  
TITLE: Expression of the multidrug resistance  
transporter NorA from *Staphylococcus*  
*aureus* is modified by a two-component regulatory  
system.  
AUTHOR: Fournier B; Aras R; Hooper D C  
CORPORATE SOURCE: Infectious Disease Division and Medical Services,  
Massachusetts General Hospital, Harvard Medical School,  
Boston, Massachusetts 02114-2696, USA.  
CONTRACT NUMBER: AI23988 (NIAID)  
SOURCE: Journal of bacteriology, (2000 Feb) 182 (3) 664-71.  
Journal code: 2985120R. ISSN: 0021-9193.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200002  
ENTRY DATE: Entered STN: 20000218  
Last Updated on STN: 20000218  
Entered Medline: 20000210

L20 ANSWER 43 OF 59 MEDLINE on STN

DUPLICATE 3

ACCESSION NUMBER: 2000138359 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10672179  
TITLE: A genomic analysis of two-component signal transduction in  
*Streptococcus pneumoniae*.  
AUTHOR: Throup J P; Koretke K K; Bryant A P; Ingraham K  
A; Chalker A F; Ge Y; Marra A; Wallis N G; Brown  
J R; Holmes D J; Rosenberg M; Burnham M K  
CORPORATE SOURCE: Anti-infectives Research; Bioinformatics, SmithKline  
Beecham Pharmaceuticals Research and Development, 1250 S.  
Collegeville Road, Collegeville, PA 19426, USA.  
SOURCE: Molecular microbiology, (2000 Feb) 35 (3) 566-76.  
Journal code: 8712028. ISSN: 0950-382X.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200003  
ENTRY DATE: Entered STN: 20000407  
Last Updated on STN: 20000407  
Entered Medline: 20000328

L20 ANSWER 44 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:156175 HCAPLUS  
DOCUMENT NUMBER: 133:115743  
TITLE: Identification of the Up- and Down-Regulated Genes in

Vancomycin-Resistant *Staphylococcus aureus* Strains Mu3 and Mu50 by cDNA Differential Hybridization Method  
AUTHOR(S): Kuroda, Makoto; Kuwahara-Arai, Kyoko; Hiramatsu, Keiichi  
CORPORATE SOURCE: Department of Bacteriology, Faculty of Medicine, Juntendo University, Bunkyo-ku, Tokyo, 113-8421, Japan  
SOURCE: Biochemical and Biophysical Research Communications (2000), 269(2), 485-490  
CODEN: BBRCA9; ISSN: 0006-291X  
PUBLISHER: Academic Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT.

L20 ANSWER 45 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
DUPLICATE 4  
ACCESSION NUMBER: 1999-12556 BIOTECHDS  
TITLE: Novel histidine-kinase polynucleotides and polypeptides used to screen for antibacterial compounds; recombinant histidine-kinase, nucleic acid, antibody and antagonist used in disease diagnosis, therapy, gene therapy and nucleic acid vaccine  
AUTHOR: Wallis N G; Shilling L K; Mooney J L; Debouck C; Zhong Y; Jaworski D D; Wang M; Throup J P  
PATENT ASSIGNEE: SK-Beecham  
LOCATION: Philadelphia, PA, USA.  
PATENT INFO: WO 9936508 22 Jul 1999  
APPLICATION INFO: WO 1999-US610 12 Jan 1999  
PRIORITY INFO: US 1998-6627 13 Jan 1998  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1999-444390 [37]

L20 ANSWER 46 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
DUPLICATE 5  
ACCESSION NUMBER: 1999-08025 BIOTECHDS  
TITLE: New *Staphylococcus aureus* histidine-kinase (HK) polypeptide and polynucleotides, useful for screening for antibiotics and for diagnosis, prevention and treatment of Staphylococci infections; recombinant enzyme production via vector-mediated gene transfer and expression in a bacterium, antisense, antibody and antagonist for gene therapy and nucleic acid vaccine  
AUTHOR: Traini C M; Kosmatka A L; Shilling L K; Warren R L; Wallis N G  
PATENT ASSIGNEE: SK-Beecham  
LOCATION: Philadelphia, PA, USA; Brentford, UK.  
PATENT INFO: EP 911406 28 Apr 1999  
APPLICATION INFO: EP 1998-305806 21 Jul 1998  
PRIORITY INFO: US 1997-963901 4 Nov 1997; US 1997-54073 29 Jul 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1999-246418 [21]

L20 ANSWER 47 OF 59 HCPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 1999:421810 HCPLUS  
DOCUMENT NUMBER: 131:69294  
TITLE: *Staphylococcus* histidine protein kinase gene *espB* and response regulator gene *espA* and methods for screening

for antibacterial agents and for treating bacterial  
 infections  
 INVENTOR(S) : Benton, Bret; Malouin, Francois; Martin, Patrick K.;  
 Schmid, Molly B.; Sun, Dongxu  
 PATENT ASSIGNEE(S) : Microcide Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 108 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932657	A1	19990701	WO 1997-US23912	19971223
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9859033	A1	19990712	AU 1998-59033	19971223
US 6514746	B1	20030204	US 1998-82077	19980520
PRIORITY APPLN. INFO.:			US 1995-3798P	P 19950915
			US 1995-9102P	P 19951222
			US 1996-713718	A2 19960913
			WO 1997-US23912	A 19971223
REFERENCE COUNT:	4	THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

L20 ANSWER 48 OF 59 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 1999:219876 HCAPLUS  
 DOCUMENT NUMBER: 130:247875  
 TITLE: Polynucleotide and polypeptide sequences from  
*Staphylococcus aureus*  
 expressed in infected tissue  
 INVENTOR(S) : Lonetto, Michael Arthur; Warren, Patrick Vernon;  
 Burnham, Martin Karl Russel  
 PATENT ASSIGNEE(S) : Smithkline Beecham Corporation, USA; Smithkline  
 Beecham Plc  
 SOURCE: Eur. Pat. Appl., 70 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 905243	A2	19990331	EP 1998-306185	19980803
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2239817	AA	19990205	CA 1998-2239817	19980805
JP 11155586	A2	19990615	JP 1998-255927	19980805
PRIORITY APPLN. INFO.:			US 1997-55387P	P 19970805

L20 ANSWER 49 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
 DUPLICATE 6  
 ACCESSION NUMBER: 1998-09561 BIOTECHDS  
 TITLE: New DNA encoding *Staphylococcus aureus*  
*histidine-kinase*,  
 used to screen compounds for antibiotic activity and as

vaccines and to treat *Staphylococcus* infection in e.g.  
wounds and prostheses

AUTHOR: Wallis N G; Shilling L K; Warren R L  
PATENT ASSIGNEE: SK-Beecham  
LOCATION: Philadelphia, PA, USA; Brentford, Middlesex, UK.  
PATENT INFO: EP 857787 12 Aug 1998  
APPLICATION INFO: EP 1998-300829 4 Feb 1998  
PRIORITY INFO: US 1997-37856 7 Feb 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1998-416009 [36]

L20 ANSWER 50 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 1998-11158 BIOTECHDS

TITLE: DNA encoding staphylococcal histidine-  
kinase;  
*Staphylococcus aureus*  
recombinant protein preparation, DNA probe, and  
antagonist, used as antibiotic or for infectious disease  
therapy, gene therapy or nucleic acid vaccine, etc.

AUTHOR: Wallis N G  
PATENT ASSIGNEE: SK-Beecham  
LOCATION: Philadelphia, PA, USA; Brentford, UK.  
PATENT INFO: EP 870831 14 Oct 1998  
APPLICATION INFO: EP 1998-302776 8 Apr 1998  
PRIORITY INFO: US 1997-43489 10 Apr 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1998-523158 [45]

L20 ANSWER 51 OF 59 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN  
ACCESSION NUMBER: 1998-10739 BIOTECHDS

TITLE: New DNA encoding *Staphylococcus aureus*  
histidine-kinase used to prevent, treat,  
diagnose and vaccinate;  
against respiratory tract infection, cardiac,  
gastrointestinal, central nervous system, eye, kidney,  
urinary tract, skin, bone and joint disorder

AUTHOR: Wallis N G  
PATENT ASSIGNEE: SK-Beecham  
LOCATION: Philadelphia, PA, USA; Brentford, UK.  
PATENT INFO: EP 863208 9 Sep 1998  
APPLICATION INFO: EP 1998-301167 17 Feb 1998  
PRIORITY INFO: US 1997-39478 25 Feb 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1998-458839 [40]

L20 ANSWER 52 OF 59 MEDLINE on STN

ACCESSION NUMBER: 1998294055 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9632266  
TITLE: Transmembrane topology and histidine protein kinase  
activity of AgrC, the agr signal receptor in  
*Staphylococcus aureus*.  
AUTHOR: Lina G; Jarraud S; Ji G; Greenland T; Pedraza A; Etienne J;  
Novick R P; Vandenesch F  
CORPORATE SOURCE: UPRES EA1655, Faculte de Medecine Laennec, Lyon, France..  
geralina@univ-lyon1.fr  
SOURCE: Molecular microbiology, (1998 May) 28 (3) 655-62.  
Journal code: 8712028. ISSN: 0950-382X.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199809  
ENTRY DATE: Entered STN: 19981006  
Last Updated on STN: 19981006  
Entered Medline: 19980924

L20 ANSWER 53 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN

ACCESSION NUMBER: 1998:927981 SCISEARCH  
THE GENUINE ARTICLE: 143UN

TITLE: Evidence for common sites of contact between the antisigma factor SpoIIAB and its partners SpoIIAA and the developmental transcription factor sigma(F) in *Bacillus subtilis*

AUTHOR: Garsin D A; Paskowitz D M; Duncan L; Losick R (Reprint)  
CORPORATE SOURCE: HARVARD UNIV, BIOL LABS, DEPT MOL & CELLULAR BIOL, 16 DIVERS AVE, CAMBRIDGE, MA 02138 (Reprint); HARVARD UNIV, BIOL LABS, DEPT MOL & CELLULAR BIOL, CAMBRIDGE, MA 02138 USA

COUNTRY OF AUTHOR: USA  
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (4 DEC 1998) Vol. 284, No. 3, pp. 557-568.  
Publisher: ACADEMIC PRESS LTD, 24-28 OVAL RD, LONDON NW1 7DX, ENGLAND.  
ISSN: 0022-2836.

DOCUMENT TYPE: Article; Journal  
FILE SEGMENT: LIFE  
LANGUAGE: English  
REFERENCE COUNT: 50

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L20 ANSWER 54 OF 59 MEDLINE on STN  
ACCESSION NUMBER: 1998294999 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9631538  
TITLE: Cloning and characterization of an accessory gene regulator (agr)-like locus from *Staphylococcus epidermidis*.

AUTHOR: Van Wamel W J; van Rossum G; Verhoef J;  
Vandenbroucke-Grauls C M; Fluit A C  
CORPORATE SOURCE: Eijkman-Winkler Institute for Microbiology, Infectious Diseases and Inflammation, Utrecht University, Netherlands.. w.j.b.vanwamel@labazu.nl  
SOURCE: FEMS microbiology letters, (1998 Jun 1) 163 (1) 1-9.  
Journal code: 7705721. ISSN: 0378-1097.

PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-Z49220  
ENTRY MONTH: 199807  
ENTRY DATE: Entered STN: 19980716  
Last Updated on STN: 19980716  
Entered Medline: 19980709

L20 ANSWER 55 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation.  
on STN

ACCESSION NUMBER: 1998:14702 SCISEARCH  
THE GENUINE ARTICLE: YL836

TITLE: KapB is a lipoprotein required for KinB signal transduction and activation of the phosphorelay to sporulation in *Bacillus subtilis*

AUTHOR: Dartois V; Djavakhishvili T; Hoch J A (Reprint)  
CORPORATE SOURCE: SCRIPPS CLIN & RES INST, DEPT MOL & EXPT MED, DIV CELLULAR BIOL, 10550 N TORREY PINES RD, LA JOLLA, CA 92037 (Reprint); SCRIPPS CLIN & RES INST, DEPT MOL & EXPT MED, DIV CELLULAR BIOL, LA JOLLA, CA 92037

COUNTRY OF AUTHOR: USA

SOURCE: MOLECULAR MICROBIOLOGY, (DEC 1997) Vol. 26, No. 5, pp. 1097-1108.

Publisher: BLACKWELL SCIENCE LTD, OSNEY MEAD, OXFORD, OXON, ENGLAND OX2 0EL.

ISSN: 0950-382X.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 39

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L20 ANSWER 56 OF 59 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 95:267936 SCISEARCH

THE GENUINE ARTICLE: QR556

TITLE: THE GENES INVOLVED IN PRODUCTION OF AND IMMUNITY TO SAKACIN-A, A BACTERIOCIN FROM LACTOBACILLUS-SAKE LB706

AUTHOR: AXELSSON L (Reprint); HOLCK A

CORPORATE SOURCE: NORWEGIAN FOOD RES INST, MATFORSK, OSLOVEIEN 1, N-1430 AS, NORWAY (Reprint)

COUNTRY OF AUTHOR: NORWAY

SOURCE: JOURNAL OF BACTERIOLOGY, (APR 1995) Vol. 177, No. 8, pp. 2125-2137.

ISSN: 0021-9193.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: ENGLISH

REFERENCE COUNT: 56

\*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

L20 ANSWER 57 OF 59 MEDLINE on STN

ACCESSION NUMBER: 94161498 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8117074

TITLE: The gene encoding plantaricin A, a bacteriocin from Lactobacillus plantarum C11, is located on the same transcription unit as an agr-like regulatory system.

AUTHOR: Diep D B; Havarstein L S; Nissen-Meyer J; Nes I F

CORPORATE SOURCE: Laboratory of Microbial Gene Technology, Agricultural University of Norway, As.

SOURCE: Applied and environmental microbiology, (1994 Jan) 60 (1) 160-6.

Journal code: 7605801. ISSN: 0099-2240.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: GENBANK-X75323

ENTRY MONTH: 199403

ENTRY DATE: Entered STN: 19940406

Last Updated on STN: 19950206

Entered Medline: 19940328

L20 ANSWER 58 OF 59 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 1994:191537 BIOSIS

DOCUMENT NUMBER: PREV199497204537

TITLE: Identification of a two-component regulatory system in *Staphylococcus aureus* that controls the expression of surface components.

AUTHOR(S): Bayles, Kenneth W.

CORPORATE SOURCE: UMBC, Baltimore, MD 21228, USA

SOURCE: Journal of Cellular Biochemistry Supplement, (1994) Vol. 0, No. 18 PART A, pp. 44.

Meeting Info.: Keystone Symposium on Molecular Events in

Microbial Pathogenesis. Santa Fe, New Mexico, USA. January 8-14, 1994.  
ISSN: 0733-1959.  
DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 2 May 1994  
Last Updated on STN: 3 May 1994

L20 ANSWER 59 OF 59 MEDLINE on STN  
ACCESSION NUMBER: 94028916 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8215360  
TITLE: Cloning and nucleotide sequence of a gene from *Lactobacillus sake* Lb706 necessary for sakacin A production and immunity.  
AUTHOR: Axelsson L; Holck A; Birkeland S E; Aukrust T; Blom H  
CORPORATE SOURCE: MATFORSK, Norwegian Food Research Institute, As.  
SOURCE: Applied and environmental microbiology, (1993 Sep) 59 (9) 2868-75.  
Journal code: 7605801. ISSN: 0099-2240.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
OTHER SOURCE: GENBANK-X62978; GENBANK-X62979; GENBANK-X62980;  
GENBANK-X62981; GENBANK-X62986; GENBANK-X62987;  
GENBANK-X62988; GENBANK-X62989; GENBANK-X62990;  
GENBANK-Z21855  
ENTRY MONTH: 199311  
ENTRY DATE: Entered STN: 19940117  
Last Updated on STN: 19950206  
Entered Medline: 19931110

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(FILE 'HOME' ENTERED AT 11:59:47 ON 12 NOV 2004)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 12:00:12 ON 12 NOV 2004

L1 1253188 S KINASE?  
L2 182160 S HISTIDINE  
L3 4732 S L1(A)L2  
L4 6785689 S CLON? OR EXPRESS? OR RECOMBINANT  
L5 249014 S STAPHYLOCOCCUS (A)AUREUS  
L6 163 S L3 AND L5  
L7 102 S L4 AND L6  
L8 58 DUP REM L7 (44 DUPLICATES REMOVED)  
E WALLIS N G/AU  
L9 119' S E3  
E SHILLING L K/AU  
L10 93 S E3-E9  
E MOONEY J L/AU  
L11 63 S E3  
E DEBOUCK C/AU  
L12 416 S E3  
L13 612 S E3-E8  
E ZHONG Y Y/AU  
L14 40 S E3  
E JAWORSKI D D/AU  
L15 276 S E3-E10  
E WANG M/AU  
L16 6684 S E3

E THROUP J P/AU  
L17 115 S E3-E7  
L18 7894 S L8 OR L9 OR L10 OR L11 OR L13 OR L14 OR L15 OR L16 OR L  
L19 72 S L6 AND L18  
L20 59 DUP REM L19 (13 DUPLICATES REMOVED)

	Issue Date	Pages	Document ID	Title
1	20040513	163	US 20040091856 A1	DNA sequences from staphylococcus aureus bacteriophage 44AHJD that encode anti-microbial polypeptides
2	20030911	65	US 20030171563 A1	Regulators of bacterial virulence factor expression
3	20030313	24	US 20030049706 A1	Novel histidine kinase
4	20021226	158	US 20020197605 A1	Novel Polynucleotides
5	20020523	20	US 20020061572 A1	Histidine kinase
6	20020110	17	US 20020004214 A1	Method to detect modulators of histidine kinases
7	20041005	151	US 6800744 B1	Nucleic acid and amino acid sequences relating to Streptococcus pneumoniae for diagnostics and therapeutics
8	20031007	88	US 6630583 B1	Antibiotics and methods of using the same
9	20030624	243	US 6583275 B1	Nucleic acid sequences and expression system relating to Enterococcus faecium for diagnostics and therapeutics
10	20030415	18	US 6548281 B1	Histidine kinase
11	20021224	19	US 6498234 B1	Compounds
12	20020625	17	US 6410263 B1	Histidine kinase
13	20010807	22	US 6270992 B1	Histidine kinase of Staphylococcus aureus
14	20010529	18	US 6238885 B1	Histidine kinase

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15	20010227	16	US 6194174 B1	Histidine kinase, 636 HK, of staphylococcus aureus
16	20001003	19	US 6127147 A	Sensor histidine kinase of Staphylococcus Aureus
17	20000606	21	US 6071894 A	Sensor histidine kinase of Staphylococcus aureus

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9	20010807	22	US 6270992 B1	Histidine kinase of <i>Staphylococcus aureus</i>
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	L #	Hits	Search Text
1	L1	15510	staphylococcus adj aureus
2	L2	285	histidine adj kinase\$2
3	L3	17	11 same 12
4	L4	67629 8	clon\$3 or express\$3 or recombinant
5	L5	12	13 same 14
6	L6	10471 6	WALLIS SHILLING MOONEY ZHONG JAWORSKI WANG THROUP
7	L7	11	13 and 16